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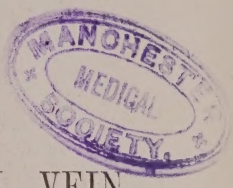

VOL. IX.

DISEASES OF THE LIVER AND PORTAL VEIN.

WITH THE CHAPTER RELATING TO

INTERSTITIAL PNEUMONIA.

BY

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LONDON:
SAMPSON LOW, MARSTON, SEARLE, & RIVINGTON.
CROWN BUILDINGS, 188 FLEET STREET.
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CONTENTS.

PONFICK.

PAGE

ANATOMICO-PHYSIOLOGICAL INTRODUCTION 3

Topography of the liver 4

Structure of the liver 6

Function of the liver 8

Jaundice 10

I. Hepatogenous cholæmia 12

II. Hematogenous cholæmia 24

(Translated by Arthur H. Nichols, M.D.)

THIERFELDER.

PHYSICAL DIAGNOSIS 33

Preliminary observations 33

Floating liver 48

Hyperæmia of the liver 57

Etiology 57

Anatomical changes 66

Symptoms 69

Course, duration, etc. 74

Diagnosis 76

Treatment 77

Hemorrhage of the liver 83

Perihepatitis 84

Suppurative inflammation of the liver 88

Historical account 89

PAGE

Etiology ... 90
Pathology ... 113
Complications ... 139
Diagnosis ... 140
Course, prognosis, etc. ... 144
Treatment ... 152
Cirrhosis or interstitial inflammation of the liver ... 166
I. *Usual form of interstitial hepatitis* ... 166
Historical account ... 167
Etiology ... 168
Pathology ... 175
Complications ... 198
Diagnosis ... 201
Course, prognosis, etc ... 204
Treatment ... 206
II. *Rarer forms of interstitial hepatitis* ... 211
Interstitial hepatitis arising from affections of the gall-ducts ... 213
Hypertrophic cirrhosis ... 217
Syphilitic hepatitis ... 222
Acute atrophy of the liver ... 238
Historical account ... 241
Etiology ... 242
Pathology ... 248
Diagnosis ... 298
Duration, prognosis ... 301
Treatment ... 304
Simple atrophy of the liver ... 305
Hypertrophy of the liver ... 313

(Translated by Arthur H. Nichols, M.D.)

VON SCHUEPPEL.

Pathological Anatomy of Cancer of the Liver ... 321
1. *Primary cancer of the liver* ... 323
2. *Secondary cancer of the liver* ... 330
3. *Pigment cancer.—Melano-sarcoma* ... 343
4. *Adenoma of the liver (adenoid liver)* ... 350
5. *Sarcoma and related forms* ... 353

(Translated by Hamilton Osgood, M.D.)

LEICHTENSTERN.

PAGE

Clinical Aspects of Cancer of the Liver 359
Historical sketch 360
Etiology 361
Symptoms and diagnosis 368
Duration 401
Termination and prognosis 402
Treatment 404

(Translated by Hamilton Osgood, M.D.)

VÓN SCHUEPPEL.

Amyloid Degeneration of the Liver; Fatty Liver; Pigment Liver 407

I. Amyloid Degeneration.

Literature and historical sketch 407
Etiology 412
Pathological anatomy 417
Pathology 428
Diagnosis 433
Duration, prognosis, etc 435
Therapeutics 437

II. Fatty Infiltration.

Description of the disease 439
Etiology 444
Pathological anatomy 457
Pathology 462
Diagnosis 468
Duration, prognosis, etc 469
Therapeutics 470

III. Pigment Liver; Melanæmic Liver.

Pathology and treatment 473

(Translated by Edward W. Schauffler, M.D.)

HELLER.

The Parasites of the Liver 483
Echinococcus 483
Other parasites 492

(Translated by Edward W. Schauffler, M.D.)

VON SCHUEPPEL.

PAGE

DISEASES OF THE BILIARY PASSAGES AND PORTAL VEIN..... 499

I. DISEASES OF THE BILIARY PASSAGES.

Anatomo-physiological remarks..... 500
Catarrhal inflammation of the biliary canals..... 509
Etiology..... 511
Pathological anatomy..... 515
Symptomatology..... 520
Complications and sequelæ..... 524
Diagnosis..... 525
Duration, prognosis, etc..... 527
Treatment..... 529
Purulent and ulcerative inflammation of the biliary canals..... 534
Etiology..... 536
Pathological anatomy..... 541
Symptoms..... 550
Diagnosis..... 553
Duration and course..... 554
Prognosis..... 555
Treatment..... 556
Croup of the biliary passages..... 557
Hemorrhage of the biliary passages..... 561
New-growths of the biliary passages..... 566
Etiology..... 572
Symptoms and diagnosis..... 574
Duration, prognosis, etc..... 576
Treatment..... 576
Disorders in the canalization of the biliary passages..... 576
Stenosis and occlusion of the biliary ducts..... 578
Etiology..... 579
Pathological anatomy..... 595
Pathology..... 601
Diagnosis..... 613
Course, terminations, etc..... 626
Prognosis..... 629
Treatment..... 630
Dilatation of the gall-bladder..... 632
Etiology..... 633
Pathological anatomy..... 636
Symptom sand diagnosis..... 638

PAGE

Course, prognosis, etc. ... 642
Treatment ... 645
Dilatation of the bile-ducts ... 649
Disturbances in the continuity of the biliary passages ... 650
1. Perforations ... 651
2. Ruptures ... 656
3. Biliary fistulæ ... 659
Parasites of the biliary passages ... 669
1. Distoma hepaticum and distoma lanceolatum ... 670
2. Ascaris lumbricoides ... 675
3. Echinococcus ... 683

(Translated by * * * * * * * *.)

Gall-stones.—Cholelithiasis ... 686
History ... 688
Physical characteristics of gall-stones ... 690
Chemical composition of gall-stones ... 696
Mode of origin of gall-stones ... 700
Etiology ... 706
Pathology and pathological anatomy ... 715
Symptomatology ... 742
Biliary colic ... 744

(Translated by Edward W. Schauffler, M.D.)

Diagnosis ... 759
Course, prognosis, etc. ... 764
Treatment ... 766

II. Diseases of the Portal Vein.

Historical sketch ... 777
Anatomical and physiological remarks ... 779
Thrombosis and occlusion ... 785
Etiology ... 787
Pathological anatomy ... 793
Pathology ... 798
Diagnosis ... 802
Course, prognosis, etc. ... 803
Treatment ... 804
Purulent inflammation ... 805
Etiology ... 807
Pathological anatomy ... 813
Pathology ... 815
Diagnosis ... 822

PAGE

Course and prognosis 825
Treatment 826
Cancer 826
Dilatation of the portal vein 830
Calcification and ossification of the portal vein 830
Rupture of the portal vein 831
Foreign bodies, gall-stones, etc., in the portal vein 832
Phlebitis hepatica 833
Aneurism of the hepatic artery 834

(Translated by * * * * * * * *.)

JUERGENSEN.

INTERSTITIAL PNEUMONIA 839
History 840
Etiology 846
Environment and occupation 864
Pathological anatomy 864

(Translated by Walter Mendelson, M.D.)

Pathology 872
General clinical history 873
Diagnosis and prognosis 902
Therapeutics 906

(Translated by Edward W. Schauffler, M.D.)

INDEX 917

ANATOMICO-PHYSIOLOGICAL

INTRODUCTION

TO

DISEASES OF THE LIVER AND ICTERUS.

PONFICK.

ANATOMICO-PHYSIOLOGICAL INTRODUCTION.

THE liver, the most extensive gland in the human body, is distinguished as much by the diversity of its relations to other organs as by its functional importance. Its extensive connections with the largest serous cavity of the body render the disturbances which take place in it of importance, not only as regards the gland itself, but likewise with respect to their influence upon the surrounding organs; though, on the other hand, changes in these may in their turn cause disturbances in the liver.

The cycle of these pathological possibilities is, however, notably enlarged by the fact that the organ may undergo considerable change in its relative position, in consequence of which its lower portion, or, as the phrase is, its lower edge, may move up and down over a considerable space. It is true that the upper and posterior portions, presenting as they do the only fixed point, are not entirely insensible to processes going on in their vicinity, as is especially shown in the history of empyema upon the right side, and in the development of large renal tumors; but all these deviations appear quite unimportant as compared with those occasionally exhibited by the anterior and lower portions, which, hanging loose in the abdominal cavity, are much more freely movable.

To these topographical conditions predisposing to pathological changes are to be added still other favoring influences, viz., the peculiar structure of the hepatic parenchyma, its mighty

development, and the remarkable duplicate character of its vascular system, from which results the tendency manifested by the liver to sympathize in the slight fluctuations which take place either in the general or in the abdominal supply of blood. In these causes lies the explanation of the interdependence, sometimes active, sometimes passive, existing between the changes that occur in diseases of the liver and those that occur in other organs; in them also must we seek for the reason why this gland when deranged not only reacts upon the condition of the blood and other parts, but also is affected more than almost any other organ by the various alterations of the blood and of the tissue changes, thereby serving as their indicator or measure. Bearing this in mind, we will now proceed to indicate the value of an accurate knowledge of the topographical as well as of the anatomico-histological relations of the liver.

Topography of the Liver.

Although very considerable disorganization of the liver may exist without influence upon its position and dimensions, still an accurate determination of its limits under all conditions is the first requisite in every examination; on the other hand, it must be understood that we are not warranted in assuming the absence of every anomaly even when both these conditions are found to be normal.

The liver fills up the cavity of the right hypochondrium, and is usually so completely covered by the arch of the ribs that only a portion of the left lobe lies directly in contact with the anterior abdominal wall, and is consequently visible after opening the abdominal cavity. The upper border is much more constant in its position, corresponding with that of the diaphragm; at its highest point it is situated at the level of the cartilage of the fourth rib.

The unequally variable lower margin coincides sometimes with the edge of the ribs, but more frequently extends from two to four centimetres beyond and in a line parallel with it. In the axillary line the lower edge of the liver, if situated high up, lies

in the tenth, or, if low down, in the eleventh intercostal space, or even lower; in adult men these last measurements are liable to many variations, which are still more numerous when the two sexes are compared, and when children are taken into account. In women, as also in children, the portion extending beyond the edge of the ribs must, in consequence of their lesser height, as well as of the incomplete development of the thorax, be considerably higher.

The left lobe, which occupies the upper part of the so-called pit of the stomach, and extends over the lesser curvature and *pars pylorica* and the first portion of the duodenum, is subject to great variations in size and form; while frequently, being short and compressed, it extends but slightly or not at all into the left hypochondrium; at other times, when thin and extended, it stretches out in a tongue-shaped projection as far as the spleen. In the median line the lower edge lies usually a little above the middle of a line connecting the point of the xiphoid process with the navel, and extends from this point more or less obliquely upward.

It is important to bear in mind that, when the liver is removed from the body, its relative form and size vary very decidedly from that observed when the organ is *in situ*, the variation being greater here than in any other organ, excepting perhaps the brain. This fact demands most careful consideration when the observations during life are to be compared with and verified by those made *post-mortem*. When taken from the body the organ becomes generally broader and flatter, the anterior convexity and the posterior concavity diminishing in depth by as much as is gained in breadth.

To give in figures the dimensions of the so-called normal liver, is very difficult, since, apart from age and stature, great variations are observed even in perfectly healthy individuals. In middle life its weight varies, according to Frerichs, from 0.82 to 2.1 kilogrammes (1.8 to 4.6 pounds); its relative weight, as compared to the whole weight of the body, being between $\frac{1}{24}$ and $\frac{1}{40}$. As a general rule, the relative weight diminishes with advancing age, a very considerable difference existing even between the volume of the fœtal liver and that of the new-born.

The Structure of the Liver

is, at least in man and the higher animals, so very different from that of all other glands, that the pathological processes which take place in its parenchyma manifest in many respects peculiar characteristics.

The structural units, *the acini*, are not bounded and enclosed by a well-marked layer of connective tissue, as is the case elsewhere, but are grouped together, standing in immediate contact, except in so far as they are separated from each other by the blood-conducting network of the *ramifications of the portal vein.* Although these "interlobular" branches of the portal vein, together with the corresponding branches of the hepatic artery and the gall ducts, run invested in a sheath of connective tissue, still this interstitial structure forms nothing more than a very wide-meshed curtain between two adjoining lobuli. Inasmuch as the portal ramifications assume uniformly a circular course, it follows that the elliptically rounded acini are surrounded by rings or hoops whose separate segments are connected by short cross-pieces.

The arrangement of the efferent vascular system of the *hepatic vein* differs in every way from that of the above-mentioned afferent blood-vessels; while the latter pass only to the periphery of each acinus, encircling it like a sinus, the hepatic vein passes through the middle of its substance from above or below in the line of its greatest diameter, forming the *vena intralobularis* or *centralis.*

The connection between these two sets of vessels is formed by the *capillaries*, which lie close to each other, penetrating the acinus most generally along the radial lines, and converging from the portal ring toward the middle, which is represented by the collecting vessel of the hepatic vein. While, however, they leave the *vena interlobularis* at almost a right angle, they join the intralobularis at an acute one, and hence resemble a very close, tree-like ramification.

The meshes of this capillary network are completely filled by the secretory elements known as the *hepatic cells.* Most of these

meshes are so narrow that they afford space for one only of these cells, which is consequently encircled by the current of blood. It is not yet definitely known whether these secretory elements and the tubes which conduct to them the requisite raw material are directly in contact with one another, or whether a lymph-space surrounding the capillaries like a sheath exists between them, though the latter view would appear to be well founded when we consider our experience with reference to most other glands, and the results not only of many artificial injections, but more especially of a series of pathological observations.

The substance of the liver-cells consists in general of a granular protoplasm with one or more nuclei of a rounded elliptical form. While the peripheral layers of the protoplasm contain numerous granules that are here and there quite coarse, the inner layers, especially those lying close about the nucleus, are formed of a variable amount of a homogeneous and amorphous mass giving the reactions of hydrogen. Together with these granules of partly albuminous and partly fatty character, there are to be observed, at least in very many cells, sharp-contoured granules of bile pigment of an intense brown color.

The *bile* elaborated in the cells thus constituted is carried off through fine cylindrical tubes, originating probably in a network in the centre of each acinus, and running between each pair of hepatic cells in such a manner that the one-half belongs to one, the other half to the other cell, as if formed, therefore, by the junction of two half tubes. By this arrangement each secreting element is brought upon all sides into direct contact with its respective draining channel, and hence is in condition to pour the secretion from each of its five or six different surfaces into a special duct. These little channels, termed capillary bile ducts —concerning which it is a disputed point whether they possess a special wall, or are merely channels grooved out in the bile substance—join each other at the periphery of each acinus so as to form larger canals, the interlobular ducts, which consist of an outer layer of connective tissue and an epithelial lining of cells approximating a cubical form. Nearer the root of the liver these cells become longer and narrower, until, upon the portion of the duct outside the organ, they assume the precise character of the

intestinal epithelium. With regard to the excretion of the bile, it is worthy of note that the wall of the larger, as well as of the finer ducts is destitute of muscular constituents.

The manner in which the *deep lymphatics of the liver* originate is a question of great importance for a due comprehension of the extensive category of interstitial diseases: on the one hand, an entire series of congestive conditions (venous hyperæmia, the various forms of nutmeg liver, etc.); on the other, a variety of neoplastic processes, as, *e. g.*, the typhoid and leucæmic hepatitis;—each and all point to the presence of channels already existing between the cells and the vessels. In the first case the capillaries may be seen surrounded by the lymphatic fluid, and in the latter by newly-formed round cells, which, as they multiply, advance along these spaces. It is much easier to demonstrate the larger collecting canals, which, possessing all the characteristics of the lymphatic vessels, run in the interlobular spaces along with the portal vein, near the artery and bile-duct, and then, uniting to form the larger trunks, pass out at the *porta hepatis*. The vessels issuing from the substance of the gland, as well as the superficial ones proceeding from the peritoneal covering and the gall-bladder, enter the lymphatic glands at the *porta hepatis* and the *ligamentum hepato-duodenale*, and by their dimensions and condition give valuable indications of the degree of the circulatory disturbances which have taken place within the parenchyma.

Function of the Liver.

Although, in the light of the eminent discovery of Claude Bernard, confirmed and elaborated by numerous later investigators, the pathological ideas of the ancients—who fancied that the gland functions and processes relate exclusively to the metamorphosis of tissues—seem quite unsatisfactory, we must, nevertheless, still admit that the chief function of the liver consists in the secretion of bile.

The most obvious, and, in a certain sense, the most characteristic constituent of the bile is its *coloring matter* — bilirubin. The fact that it is identical with hæmatoïdin, the crystalline

product of stagnant extravasation, affords a significant indication of its origin. But, in this connection, it may be said that the old ideas upon this point have undergone revision; in fact, it becomes more and more certain and clear that the bile is to be regarded chiefly as a vehicle for the removal of the refuse matter of the blood, though it must be admitted that we understand but imperfectly either the intermediate and metamorphic processes of the two coloring matters, or the method of their passage from the blood into their secretory canals. Still less can we answer the question, so important for the comprehension of the entire secretory process, whether and to what extent the constituents of the bile are conveyed to the cells by the circulation, or to what extent they are furnished by the secretory elements themselves. In the chapter upon Icterus will be presented the evidence in favor of each of these possible conditions.

Besides bilirubin and some other matters, which, like cholesterin, lecithin, etc., are found already formed in the blood, the bile contains as its chief constituents two (so-called paired) acids in combination with alkalies, the glycocholic and the taurocholic acid. It is certain that these acids are not conveyed, as such, to the liver, but that they are produced in its parenchyma by the action of the hepatic cells.

The entire *quantity* of bile secreted, apart from the considerable individual variations, differs very much in proportion to the quality and quantity of the ingested food. According to the estimates of Ranke and Wittich, which agree quite closely, a man secretes during twenty-four hours about 14 grms. of bile, containing 0.44 grm. of solid matter, for every kilogramme of his weight. The secretion is increased by a meat diet, while it is diminished by fatty food; and during an exclusively fat diet it sinks to the same level as that resulting from a state of complete inanition.

In addition to the production of the bile, a second series of important processes goes on in the liver, viz., the formation of *glycogen*, the presence of which in the hepatic cells has already been alluded to. This substance is now generally considered to be formed from the hydrocarbons of the ingesta, which are carried to the liver from the intestinal tract. The direct trans-

forming action of the secretory elements (their ferments) probably changes these bodies into glycogen, which accumulates in considerable amount, varying according to the character of the food. Our knowledge of the further destiny of the bile is as yet only conjectural; for, with regard to the original view of Cl. Bernard, that during life it is changed into sugar, it has been proved that, at most, only a very insignificant portion of the glycogen undergoes this transformation *intra vitam.*

Of the two vascular systems which convey blood to the liver, that of the *arteria hepatica* is unquestionably of relatively secondary importance; the portal vein is to be considered as the chief source of the products formed by the parenchyma of the liver—both those which are at once excreted, and those which are stored up for a longer time within it, and returned to the circulation either unchanged, or in a modified form.

The essential differences which are to be observed between the morphological as well as the chemical constitution of the portal blood and that of the hepatic vein, have been uniformly regarded, since Lehmann's observations, as the result and measure of important changes within the parenchyma of the liver. The active influence of the glandular tissue is, moreover, evident from the fact that it is impossible to demonstrate in the blood of the portal vein the existence of the above-mentioned specific constituents of the bile and also of glycogen. In view of these facts, Kuehne's opinion, that it is in the liver, and in it alone, that *glycin* and *taurin*, the twin products of the metamorphosis of albumen, combine with the biliary acids, appears to be as well founded as the conclusion that the bilirubin, as such, is, under normal conditions at least, first produced in this organ.

Jaundice.

Icterus. Cholæmia.

The term *cholæmia*, in its broadest signification, indicates a condition in which the essential constituents of the bile circulate

in the blood; while by *icterus* is understood a cholæmia in which the foreign substances, especially the pigment, have passed out of the vessels into the tissues, and particularly into the outwardly visible portions of the body. Although the two terms are not unfrequently used as if perfectly interchangeable, the above distinction is not based upon theoretical grounds alone. The latter term implies that the absorption of bile-pigment by the blood is by no means necessarily followed by icterus, but that the extra-vascular tissues are not affected until this process has continued for a certain time and reached a certain stage, when that infiltration known as *jaundice* takes place in the surrounding parts. Hence, it is important to draw the line closely between these two possibilities, remembering that in certain insidious changes of the hepatic parenchyma, or in certain alterations of that tissue, unimportant in themselves, icterus may, indeed, be altogether absent, while there may be observed in the urine and also in the blood a slight trace or a transitory appearance of the constituents of the bile. But this distinction is, moreover, of direct practical utility, since, between the time of the accumulation and absorption of the bile and the appearance of icterus, a number of hours, and not unfrequently of days, must always intervene. It is certain that during this interval the fundamental condition necessary for the production of icterus is present, although the jaundice itself is still wanting, which must therefore be regarded as only one of the possible sequences of cholæmia, very frequently observed, but by no means an invariable or necessary external manifestation. The appearance of icterus always indicates one of the higher grades —a sort of cumulative stage—of the cholæmic condition of the blood, and may, hence, be regarded as a quantitatively increased cholæmia.

The presence of the biliary constituents in the blood can be brought about in two ways: either by the absorption into the circulation of bile which is already secreted, but arrested in its flow, or more directly by certain metamorphoses occurring altogether in the blood itself. Since the secretion of bile takes place only in the liver, this foreign admixture can, in the first instance, originate only in this gland—*hepatogenous cholæmia;* while, in

the latter case, it arises, according to all indications, directly and originally in the circulatory system—*hematogenous cholæmia.* These very distinct sources give rise to essential differences in the two varieties, which may very properly be employed as indications for the differential diagnosis, inasmuch as in the hepatogenous form all the constituents of the bile, especially the acids, pass into the blood, to appear, according to circumstances, in the secretions; while in the hematogenous form this is true of the bile-pigment only.

I. Hepatogenous Cholæmia.

Hepatogenous, Mechanical, Resorption or Obstruction Icterus of Authors.

Among the numerous agencies which may induce the already formed bile to pass into the circulation, an obstruction of the biliary ducts in some part of their course—either of the larger ones lying outside of the liver, or of the intra-hepatic ducts—is by far the most common. As is well known, the secretory pressure of the bile is in itself only slight; but the force of its currents would seem naturally to be doubly weak, since the walls of the efferent channels, in which, as we have seen, muscular elements are wanting, afford no acceleratory impulse; such additional impulse to the *vis a tergo* is communicated only by the respiratory action of the diaphragm, whereby the cavity of the abdomen is diminished and the mass of the liver compressed. The researches of Friedlaender and Barisch have lately shown that a moderate, opposing pressure is competent not only to arrest further secretion, but even to cause that already formed to flow back and pass over into the blood-vessels.

There occur, indeed, at times, notably in human beings, conditions, apparently very insignificant, which prelude the complicated symptoms above mentioned; among these are the catarrhal swellings of the larger bile ducts, especially of the *pars duodenalis* of the *ductus choledochus*, whereby the catarrhal form of icterus is induced. Virchow has very properly laid stress upon the fact that the obstruction of the interior of this duct by catarrhal secretion—the so-called "mucous plug"—(deemed by many

to be invariably present in this condition) is neither necessary upon theoretical grounds—even when the above-mentioned facts are considered,—nor can its presence always be demonstrated even in cases of well-marked jaundice. A moderate infiltration of the fold of the *mucosa* of the duodenum surrounding the orifice of the duct, or less frequently of the inner surface of the *choledochus* itself (as will be readily understood when we consider the peculiar operation of the biliary secretion), is much more likely to bring about this result. Such infiltration may be produced by distention of the vessels, as well as by a serous infiltration of the mucous and sub-mucous tissues. This change is from its nature so obscure as to escape an inexperienced eye; so temporary and variable as to vanish before its existence can be demonstrated by an autopsy; while, even after death, it may be modified so as to be unrecognizable. It cannot be denied that one of the chief causes of this phenomenon is the occasional closure of the duct by a small accumulation of cells of cylinder-epithelium detached from its wall, which in spite of its looseness may obstruct the flow of the contents of the duct; but such is by no means the usual occurrence.

The simplest and most obvious examples of catarrhal icterus are those which are demonstrably connected with the sub-acute form of gastro-enteritis; to this class are to be assigned those forms of icterus which appear as the sequel of a symptomatic gastro-enteritis, such as accompanies many typhoidal fevers and other infectious diseases. Under this head, moreover, are to be included those less closely allied cases, not unfrequently of unknown or obscure origin, in which the catarrhal condition makes its appearance in the finer ducts lying within the parenchyma of the liver; of the latter are the forms of icterus which accompany many traumatic diseases, epidemics of pyæmia and puerperal fever, and sometimes, but less frequently, malignant erysipelas. Although the presence of abscesses of the liver may indicate clearly the cause of the jaundice, there are, nevertheless, instances in which every agency of this sort is wanting, and no other abnormity can be found than the distention of some of the ducts from accumulated bile or rudimentary epithelium. The theory that this form of jaundice depends always upon a

catarrhal condition proceeding from the intestine, would constitute unquestionably a somewhat artificial explanation, and has hence received a qualified acceptance only; it seems far better to assume a disturbance originating in the interlobular vessels. The jaundice appearing in phosphorus-poisoning is probably to be explained in like manner, only that in this case the pressure of the greatly swollen secreting cells co-operate with the catarrh of the finer ducts; and in the same way even those of larger calibre may be compressed and a stasis produced, which in turn may give rise to the catarrhal condition. To this class also belong—according to the hypothesis of Senator—those peculiar cases in which jaundice recurs regularly at intervals of four weeks, either simultaneously with the menses, or to a certain extent in their stead—*icterus menstrualis*—and possibly, likewise, a series of other forms, the etiology of which is as yet imperfectly understood.

Precisely the same effect as is caused by the swelling of the mucosa and the enlargement of the hepatic cells may be also produced by growing neoplasms starting from the inside of the gall-duct or compressing it from the outside. The external compression occurs with comparative frequency, since the duct lies in most intimate connection with the pyloric portion of the stomach, which is so very liable to form the seat of tumors. If, now, such a growth should invade the duodenum, or—as indeed seldom happens—should orginate in that part, it may either involve the orifice of the duct, or, penetrating it, advance along its canal. This effect, however, is most frequently produced by *calculi* which give rise to an imperfect obstruction, and rarely to complete occlusion, of the duct, inducing in turn by their manifold effects results as variable as they are difficult to understand. The chief features of the affection change completely and often very suddenly, according as the calculus advances or becomes impacted; partially breaks up, or enlarges from fresh accretions; remains within the duct, or, after gradual destruction of its wall, breaks through it.

Mention should be made at this point of numerous neighboring factors which are competent to cause compression, and thereby a narrowing or obstruction: these consist most fre-

quently of tumors of the stomach, the duodenum, the head of the pancreas, and especially those formed in the liver itself, which by their irregular development tend to bulge up against the *ligamentum hepato-duodenale.* The same may be said of the different neoplastic processes, either inflammatory or in the form of tumors, which take place in the *ligamentum hepato-duodenale* itself as well as at the base of the lymphatic glands enclosed within it. The influence of more distant organs, such as the omentum, transverse colon, etc., is sometimes, though less frequently, to be taken into account; although the possibility of the accumulation within the latter of large masses of impacted fæces is to be considered, the great mobility of the transverse colon rendering it quite easy for these masses to be brought into direct contact with some part of the *ductus communis.*

All these processes, and, above all, those seated in that fold of the peritoneum containing the *ductus choledochus*, are very apt to be complicated with peritonitis — at times of an adhesive nature, at others characterized by contracting eschars; and thus is developed, as the result either of these phenomena alone, or of their after-effects, the two-fold tendency to rupture, displacement, or angular tear of the gall-duct, loosely embedded in the movable sub-serous tissue, but adherent to it only on one side. A like effect is produced in the parenchyma itself of the liver by abscesses, new-growths, cysts containing parasites, etc.; and in these cases icterus may be present or absent, in a severe or a mild form, according as these processes involve the smaller or larger gall-ducts, or are attended or not by an extension of the inflammation to their walls.

There is still another variety of this disorder which, to render this matter complete, should be briefly alluded to, and which was formerly a subject of much discussion. This comprises that form in which the icterus was thought to be attributable to spasmodic contraction, or, according to others—strangely enough — to paralysis of the walls of the gall-duct, resulting from a sudden chill, mental disturbance, and the like — *icterus spasticus* (*icterus spasmodicus*). This affords an example of one of those old theories, based not upon any adequate physiological basis, but originating in the practical demand of the moment for

an explanation of the surprisingly sudden appearance and disappearance of icterus. Since the discovery, however, that the wall of the gall-duct is quite unsupplied with the muscular elements formerly ascribed to it, the theory of *icterus spasmodicus*, which was in other respects hypothetical, has lost even the possibility of an existence; upon the other hand, the results of combined clinical and anatomical observations have afforded proof, as has already been briefly shown, that these sudden changes may be induced by a great variety of phenomena operating in a purely mechanical manner.

Somewhat more remote are the causes tending to produce that variety of icterus in which the smaller as well as the larger gall-ducts are found to be quite intact, and the hepatic tissue presents from the very outset a perfectly normal appearance, but where, on the other hand, in the *acceleration or retardation in the respiratory movement of the diaphragm* conditions are brought about sufficient to cause an obstruction to the flow of the bile. It would appear that this factor has as yet by no means attracted that careful attention which, from a pathological point of view at least, it so well deserves. And yet it would appear that many varieties, which would otherwise remain obscure, might be referable to this cause; such, for instance, as certain forms of bilious pneumonia, icterus accompanying the different affections of the lungs and pleura, and possibly also pyæmia, puerperal fever, and other diseases, so far as they are complicated with accumulations, the formation of infarctions in the lungs, or with pleuritis. A somewhat similar change can also be induced by those chronic affections which, producing indirectly a reaction toward the lungs, are followed by obstructions in the circulation, œdema, and hydrothorax. I can here only allude to those tedious cardiac troubles in which, on the one hand, the final paralysis of the heart's action and the refusal of further compensatory activity on the part of its muscular tissue, on the other the outbreak or rapid increase of œdema as well as the appearance of icterus, at length rapidly supervene, announcing the approach of a fatal termination. Under this head may possibly be included, moreover, many cases of *icterus neonatorum*, especially in children born prematurely or very

feeble, in so far as the respiration under such circumstances is but slowly and imperfectly established. It should be borne in mind, then, in all these cases, that the excretion of the bile, which, apart from the pressure induced by the presence of the secretion itself, is produced solely by the impulse communicated by the movements of the diaphragm that tend to compress the liver, may be so seriously obstructed by the withdrawal of the latter influence, that a retention of bile must supervene, though limited, indeed, to certain portions of the organ.

In addition to the varieties of obstruction above described, which rest upon an anatomical basis more or less demonstrable, there exists still another group, much smaller indeed, but commanding an especial interest, where the explanation of the phenomenon is to be sought not in any irregularity of the flow of the bile — a cause always to be taken cognizance of, — but in changes experienced in the blood-pressure of the hepatic vessels, a contingency to which attention was first directed by Frerichs.

All influences that sensibly reduce the blood-pressure in the portal vein and its ramifications must tend to favor the imbibition into the circulation of a secretion that is subject to slight excretory pressure ; and this is more likely to occur if this diminution of the blood-pressure attains of a sudden a certain degree. If this process should be generally recognized, we could not fail to be involuntarily impressed with the conviction that cholæmia attributable to this origin is of much more frequent occurrence than is denoted by the appearance of icterus ; since, as already stated, it is only the severer grades of this cholæmia, commonly of short duration, that give rise to an icteric discoloration of the superficial integument.

Among such agencies may be enumerated hemorrhage from the roots of the portal vein, and narrowing or obstruction of the calibre of its branches, which may be induced by external pressure arising from either pylethrombosis or pylephlebitis, or from the formation of tumors, concretions, etc. Frerichs has attempted, moreover, to refer those varieties of icterus, usually severe, that accompany many infectious diseases, to the diminished lateral pressure exercised upon the portal vein, resulting

either from the intestinal absorption[1] occurring at that point, or produced directly by hemorrhages from the stomach and intestines, such as are observed in yellow fever.

It is obvious that the demonstration in individual cases of the presence of anomalies of this character in the circulation is attended by great difficulties, and the more so from the fact that our knowledge respecting numerous questions relating to the normal circulatory system of the liver is as yet extremely imperfect. In fact, to this circumstance, and to the impossibility of affording an accurate anatomical demonstration of these alterations, is chiefly to be ascribed the fact, that up to the present time no distinct outlines have been assigned to the domain of this last form of icterus. It must, therefore, for the present remain also undecided whether, for example, the jaundice which forms so prominent a feature in many severe epidemics, as in *typhus recurrens*—on which account this disease was for a long time considered to possess a specific character (bilious typhoid)—is, in like manner, to be referred to this cause, or whether, as is commonly thought, it is to be regarded as simply catarrhal in its character. So, also, in case of *icterus menstrualis*, as described by Senator, there are many facts tending to favor the theory that the icterus is here produced, not by a catarrh of the biliary duct, but by sudden changes in the blood-pressure in the portal system.

As regards the precise method of the passage of the bile into the circulation, it has until recently been imagined that there occurred a stagnation of the biliary secretion in the vicinity of the capillary ramifications of the hepatic ducts, and that, as soon as this accumulation had reached a certain amount, a direct filtration occurred into the neighboring blood-capillaries. Certain objections to this method will, however, be suggested when it is remembered that there exists nowhere any immediate connection between the gall-capillaries and blood-capillaries, these vessels being everywhere separated from each other by the cellu-

[1] An example of this character, susceptible of experimental demonstration, may be found in the variety of icterus—at times quite severe, but usually somewhat variable—observable during forced deprivation of food.

lar substance of the liver, which the bile in its passage would have first of all to penetrate. It has, however, been lately demonstrated by Fleischl that, when a ligature has been applied to the *ductus choledochus* or *hepaticus*, the bile finds its way into the circulation almost exclusively by way of the thoracic duct—a somewhat circuitous route; whereas, if this latter duct be tied together with the *choledochus*, no bile whatever, or but slight traces of it, can be detected in the blood. In even the milder cases of icterus one can be convinced at a glance of the fact that the hepatic lymph assumes a perceptible yellow color, traceable into the portal gland, and even beyond. In fact, it is to experimental investigation, as it is termed, that we are indebted for the knowledge that this is the one route invariably chosen. This phenomenon throws, however, new light upon, and affords additional support to, the theory above unfolded respecting the origin of the lymphatic vessels of the liver, according to which there is also inserted in this gland, between the secretory cells and the blood-capillaries, quite an extensive system of channels for the flow of lymph.

General Symptomatology of Hepatogenous Icterus.

The phenomena resulting from a diminished flow of bile into the intestine, or from its total stoppage, are divided into those of a positive and those of a negative character. The latter group comprises the disturbances of the digestive and resorbent functions, which are invariably associated with the absence of bile from the contents of the intestine, or its insufficient admixture, and which betray their presence in a striking manner by the abnormal coloring of the fæces. This discoloration affords to physicians a valuable means of estimating the force of the agencies tending to impede the natural flow of the secretion, for it is in exceptional cases only, that the fæces continue for any length of time absolutely void of color, varying then from a pure dirt to a silver-gray color, or, more frequently, a clear, pipe-clay color, exhibiting at different times a hue of varied intensity.

The phenomena of the former (positive) class are only observed in case of occlusion of the ductus choledochus, and are attributa-

ble most frequently to the presence of calculi; they indicate the existence of an absolute obstruction. In consequence of this stoppage the fat passes through the intestines for the most part unchanged, thus giving rise to the peculiar variegated, silvery appearance of the excrements, as well as to their clayish, viscid consistence. Upon the other hand, if the biliary duct be but partially obstructed, the resorption of the fat may be readily accomplished, provided the food consumed be not excessively rich in fat.

It is, moreover, probable that to the small amount of bile mingled with the contents of the intestine is to be referred that intestinal obstruction which so frequently accompanies icterus, as likewise the tendency to flatulence and to rapid decomposition of the fæces, though the intimate relation here existing between cause and effect is not very clearly understood.

The other (positive) resulting phenomena are characterized by the presence of the constituents of bile in the blood. The presence of the coloring matter is manifested first and most obviously by the circumstance that, at the expiration of about twenty-four hours, the serum, and shortly after (in from twenty to forty hours) the walls of the vessels assume a yellowish hue, and subsequently (from forty to sixty hours) even the extra-vascular tissue becomes likewise imbued. In this manner is produced the appearance of the most prominent symptoms of cholæmia, viz., icterus or *morbus regius*. The susceptibility of the different parts of the body to impregnation with the coloring matter of the bile is very unequal. It is the greatest in case of the serous and fibrous membranes, in the thick, and especially the loosely-formed, free connective tissue; then follow the epithelial and certain glandular cells, especially those of the kidneys, whereas bones evince but a slight tendency to its absorption, and cartilage almost none whatever. Upon the other hand, the transition from the blood into the contents of the serous cavities, as well as into transudations and exudations, takes place very rapidly; the latter especially, proceeding as they do directly from the serum of the blood, constitute a very convenient means of distinguishing a mild or doubtful jaundice. According to all appearances, the coloring matter that has transuded into the tissues does not find its way back into the blood until

the quantity of this substance contained in the latter fluid itself has sensibly diminished. In this manner, then, must result gradual accumulation of the coloring matter, and an intensification of the abnormal coloration, which continues for a considerable length of time, although there may not necessarily have occurred, in the meanwhile, any increased resorption from the parenchyma of the liver into the blood. It is only after this process of absorption from the liver has ceased, or at least materially diminished, that the current begins to be reversed, by which means the gradual restoration of the normal color of the skin is brought about. The fluids found in the parenchyma contain the bilirubin not only in solution or diffusely infiltrated, but at times also in the form of distinct brown grains or masses. No permanent injury is, however, induced in the tissues thus infiltrated.

The bile-pigment having penetrated, in the manner thus described, the substance of the various tissues of the body, is subsequently eliminated from the blood, not definitively, but only to be restored, in due time, to the circulation. The obvious channels which, under ordinary circumstances, would remain open to rid the organism once and for all of its presence, are mainly the *excretory ducts* of the *kidneys* and the *sweat-glands*.

Shortly after the process of resorption has begun, the urine acquires first a saffron and then a reddish hue, subsequently becoming more and more of a brown color, exhibiting the appearance of every shade, from that of beer to an all but green tinge. The fluid is clear, transparent, and quite frothy. Although these peculiar properties indicate unmistakably the admixture of bile-pigment, it is much more difficult to demonstrate the presence of biliary acids, as is shown by the circumstance that our knowledge of their occurrence in the urine of icterus constitutes a most recent discovery, for which we are indebted to Hoppe-Seyler. Indeed, our previous ignorance in this matter is attributable partly to the fact, that a comparatively small portion of the biliary acids that have found their way along with the bile into the blood is eliminated from the economy together with the urine; whereas another and a larger quantity, that has previously passed into the circulation, undergoes transformations of

a different character. In their passage through the kidneys the constituents of the bile thus eliminated, and especially the coloring matter, give rise, in the moderately severe cases of icterus, to a variety of disturbances, affecting in part the epithelium and in part the calibre of the tubuli. The epithelium exhibits not only the various stages of granular-fatty metamorphosis, but granules and masses of pigment of various degrees of coarseness make their appearance within it; the tubuli of the cortical and medullary substances, on the other hand, are here and there distended with cylindrical casts, which are in part hyaline, though the icteric urine in which they are immersed imparts to them a light greenish hue, and in part — viz., in the severe cases of complete biliary obstruction which gives rise to the so-called *icterus viridis*—sausage-shaped plugs, from a grass-green to an almost blackish color, loosely packed together in masses, and manifesting a great capability for resisting the action of the most diverse reagents. Each variety of cylinders can appear also in the urine.

As compared with the quantity of coloring-matter which passes out through the kidneys, that eliminated by the *sweat-glands* is relatively insignificant.

It should be remarked, however, that the modes thus described, by which the blood discharges these foreign ingredients — in part temporarily and in part finally, — suffice for an adequate elimination only in case the fundamental cause does not operate for too long a time, and thus bring too severe a strain upon the depuratory capacity of the kidneys. Should the exciting cause, however, persist wholly or at least in part, then the natural tendency toward recovery is so continuously taxed by this agency that ultimately a paralysis of the depuratory function must inevitably supervene. In the usual course of severe forms of icterus, provided no other complications ensue, the moment when these compensatory agencies become exhausted constitutes the signal for a fatal termination.

It happens not unfrequently, however, that this, so to speak, favorable progress is unfavorably influenced and prematurely arrested by the disturbances produced in entirely different vital organs by the retention of the bile in the blood. This deleterious

influence makes its appearance, first of all, in the nervous and muscular systems, and manifests its presence, as was long since known, by a retardation of the pulse and respiration as well as by a considerable diminution of the temperature. Although, so far as regards the last two phenomena, the nervous system would appear to constitute the actual point of attack, the diminution in frequency of the pulse (to forty and less) would seem rather to point to a paralytic condition of the heart, such as is likewise observed throughout the entire muscular system, and the presence of which is indicated by a sensation of lassitude and exhaustion. But along with the spinal cord, the cerebrum itself, also, is sympathetically involved; of which, evidence is afforded by the cerebral irritation, convulsions, psychical exaltation, and even mental derangement, which in the later stages — those of approaching paralysis, appearing in the form of an apathetic or comatose condition—are wont to follow. It often happens that a severe derangement of the nervous system appears simultaneously with a general hyperæsthesia, whose presence is especially characterized by insomnia. The severe train of symptoms above portrayed, such as is developed and, as a rule, often repeated in the cases of so-called *icterus gravis*, is designated by the term *cholæmic intoxication.*

In the light of numerous experimental researches, the cause of all these phenomena may be attributed to the presence of the biliary acids in the blood, exerting an indirect influence, it would appear, upon the ganglionic and muscular systems. At all events, the theory that they indirectly give rise to that symptom merely by their property of destroying the red blood-corpuscles, forms an inadequate explanation, the quantity of colored cells dissolved by this agency being comparatively small. Whether, however, all the other described phenomena are likewise referable to this cause, and whether still other and more obscure symptoms—such, for instance, as the cutaneous itching and the abnormities of the sense of taste and vision [bitter taste in the mouth and xanthopsia ("yellow seeing")]—are to be explained in like manner, are problems which can no more be resolved at the present time than can the question respecting the further fate of the products of the metamorphosis of the biliary acids within the

circulatory system; for indeed only a small quantity of these acids, as we have seen, finds its way into the urine to be eliminated with that secretion, by far the greater portion undergoing additional changes. Upon the other hand, however, as regards the decided influence ascribed to the biliary acids in these nervous attacks, these phenomena have been referred to the retention of those substances which are regularly intended to be elaborated within the liver into bile and eliminated with that secretion. In case the icterus should persist for so long a period that, as a result of this prolonged biliary obstruction, a certain number of liver-cells are broken up and dissolved, or while surviving, are, nevertheless, so distended with either unelaborated or fully-formed secretory material as to be rendered incapable of further appropriation and transformation, then it is quite possible for such an accumulation of deleterious substances to be formed within the circulation as would thereby give rise to severe symptoms, the sequelæ of a more or less complete *acholia*.

Quite recently Koloman Mueller, while subjecting to experimental proof an hypothesis enunciated by Flint, proposed the theory that the appearance of cholæmic poisoning can be produced neither by bile nor by glycocholate of soda, nor, finally, by taurin; but that it is much more likely to have its origin in an abnormal increase in the quantity of cholesterin contained in the blood. A further confirmation of this theory is extremely desirable.

II. Hematogenous Cholæmia.

(Hematogenous or Blood Icterus of Authors.)

Hematogenous icterus, unlike the hepatogenous form, is characterized by a certain disturbance located, from the outset, in the blood, which gives rise to the appearance of free biliary pigment in that liquid; it runs its course quite independently of any influence exerted by the liver.

Although in the attempt to describe this variety numerous and ever recurring obstacles are encountered, now that the theories formerly advanced by Kuehne and M. Herrmann have re-

ceived repeated corroboration from the investigations of Tarchanoff and the writer's own observations, the fact of its actual existence can no longer be disputed.

After Hoppe—who was the first to detect the presence of the biliary acids in icteric urine, thereby overthrowing the hypothesis of Frerichs as to their transformation into biliary pigment—Kuehne demonstrated that the introduction of a variety of substances, possessing quite a diverse character, into the circulation might lead to the appearance of biliary pigment in the urine. Such an effect is produced by water, the biliary acids, and salts composed of biliary acids, ether, chloroform, and other substances which have in common the property of dissolving red blood-corpuscles. Inasmuch, then, as this disturbing influence is, as may be demonstrated, most potent in case of the biliary acids, Kuehne attempted to account for the production of this kind of icterus in the urine by propounding the theory that the hemoglobin, rendered free by this dissolution of the blood-globules (the presence of which can be demonstrated both optically and chemically in the plasma), is subjected within the circulation to a still further dissolution, and, after a previous transformation into bile-pigment, is eliminated by way of the urine.

There is another theory, designed to explain the origin of this form of icterus, in conformity with which the disorder is attributed to some overlooked catarrh in the capillary system of the gall-duct; or to some transient anomalies in the hepatic circulation; or, finally, to nervous influences; the correctness of this hypothesis, however, has not yet been fully demonstrated. Upon the other hand, the results obtained by Tarchanoff and the author, when injections were made of solutions of bile-pigment (obtained by freezing), or solutions of hemoglobin-crystals, are in complete harmony with the foregoing theory. There appears thereafter in the urine, first hemoglobin, and shortly after, a brownish or greenish pigment, which gives the reactions of bilirubin. Surely, therefore, there can no longer be any doubt as to the possible hematogenous character of certain varieties of icterus occurring in mankind. This form may, moreover, be especially looked for where an extensive destruction of the red blood-corpuscles has taken place.

Before proceeding to consider those morbid conditions where the existence of one of these varieties of icterus has been demonstrated or at least shown to be probable, it will not be out of place to allude to the attempt made to assign an hematogenous character to certain peculiar cases of icterus, an attempt which has found expression in the constitution of a special category, the so-called *icterus from suppression*. Proceeding upon this assumption, now known to be erroneous, it was maintained that the bile is formed as such in the blood, and, circulating with that liquid, is only to a certain extent separated from it by filtration in the liver. Starting upon these premises, in those disorders involving an extensive and at the same time rapid destruction of the secretory parenchyma, associated with severe jaundice—such as is observed in phosphorus-poisoning, acute atrophy, and many processes running a rapid course and characterized by suppuration and softening—it was not unnatural that the jaundice should be attributed to a retention of that substance already circulating in the blood. Since, however, the incorrectness of these premises has been demonstrated—that is to say, since it has been established by the experiments performed upon the lion by Johannes Mueller and Kunde, as well as by Moleschott, that the characteristic constituents of the bile are not preformed in the blood, but are prepared only in the liver by means of the specific action of its cells, the entire theory based upon the above idea has fallen to the ground. Upon the other hand, the idea upon which the conception of the icterus of suppression is based—that of the retention of certain constituents which, even though they are not eliminated from the liver as such, are, nevertheless, appropriated in the elaboration of its secretion—has acquired in the description of *acholia* a shape harmonizing with the above-mentioned experiments (compare p. 24). Indeed, in these very cases of extensive destruction of the hepatic tissues, it cannot be doubted that a large quantity of excrementitial matter, whose natural outlet is obstructed, must be retained in the blood; and it must also be admitted that this circumstance must exercise a sensible influence upon the general condition of the patient. We should, therefore, give careful consideration to the theory according to which the complex symptoms of the so-called cholæmic intoxica-

tion are ascribed in a far greater or an equal degree to acholia ; although, owing to the difficulty attending any experimental verification of these processes, it has not yet been possible to determine accurately the extent of the influence thus exerted.

It is much more difficult than would be imagined, to arrive at any absolute decision respecting the question of the existence of hematogenous icterus in mankind, because the biliary acids, whose respective presence or absence would serve as a differential standard, appear in the urine, as is well known, only in very slight quantities even in the severer varieties of hepatogenous icterus. With reference to this point, however, we should be cautious not always to regard the absence of the biliary acids as affording strong reasons for assigning to the coloring matter an hematogenous character. Upon the other hand, it is precisely in those varieties of icterus which, in accordance with a certain preconceived opinion, we have always regarded as possessing pre-eminently a hematogenous character—such, for instance, as the icterus of pyæmia — that the concomitant presence of biliary acids in the urine has been repeatedly demonstrated. Indeed, in view of the above detailed account of the varied contingencies in which the liver may exert an influence in inducing those phenomena, this circumstance can hardly surprise us, and, furthermore, cannot alone furnish any evidence tending to disprove the idea that in certain peculiar cases of pyæmia an icterus of a hematogenous character may occur; it simply indicates that certain individual cases of icterus may have possessed an hepatogenous character. It will be understood that still less assistance is here obtained in determining whether, perchance, in addition to the hepatogenous icterus, the hematogenous form may not, at the same time, have run its course, the latter being to a certain extent independent of the former.

As regards, therefore, the theory that jaundice in pyæmia may under certain circumstances be of the hepatogenous form, and under others of the hematogenous, it may be affirmed that this view is not only possible, but quite probable. Further observations, however, conducted independently and with the greatest accuracy, can alone assign definitely to each class its own appropriate boundaries.

Among the affections, then, to which a hematogenous origin may with more or less probability be assigned, may be mentioned: many infectious diseases, especially typhus and swamp fever, yellow fever, and likewise a variety of disorders due to the effects of poison (sulphuric, phosphoric, and arsenious acid, snake-bites, etc.), and, finally, possibly *icterus neonatorum*. It has already been stated that to the icterus of phosphorus-poisoning, which has by some authorities been relegated to this variety, a mechanical origin ought really to be assigned.

Symptomatology of Hematogenous Icterus.

It will be readily understood that the consecutive symptoms produced by hematogenous jaundice must be materially different from those of the hepatogenous form, for we have here to deal simply with the presence of biliary pigment in the blood. We shall have occasion to note the absence of the negative symptoms observed in the latter variety, and, above all, the absence of bile in the contents of the bowels, and the effects of this deficiency, as well as those positive phenomena that may be induced by the presence of the biliary acids, the cholesterin, etc., in the blood.

Both these phenomena possess a diagnostic significance that should not be underestimated, but for similar reasons are not pathognomonic, as there may occur also cases of hepatogenous icterus where the dejecta are still colored, the urine free from biliary acids, and where the typical picture of cholæmia has not —or, more correctly perhaps, has not as yet—been developed.

Upon the other hand, however, there may be observed in the hematogenous, as in the other form, all the symptoms produced by the presence of bilirubin — the coloring of the plasma and rarely, also, of the tissues and the yellowish tinge of the external parts thereby caused, as also the icteric coloration of the parenchyma of the kidneys, and, finally, the presence of biliary pigment in the urine. There are absent, on the contrary, all those remains so striking to the eye which in cases of retention of the bile are left behind in the hepatic parenchyma, and, above all,

moreover, that fundamental pain in this organ and its appendages.

As regards the general features of the affection, it has not yet been found possible to single out any group of symptoms, constantly and decidedly characteristic, which may, beyond question, be attributed purely to the icterus, and which are not connected in some way with the primary disorder that is commonly quite severe.

PRELIMINARY PHYSICO-DIAGNOSTIC

OBSERVATIONS

UPON

DISEASES OF THE LIVER.

FLOATING LIVER, HYPEREMIA OF THE LIVER, PERIHEPATITIS, SUPPURATIVE HEPATITIS, INTERSTITIAL HEPATITIS, SYPHILITIC HEPATITIS, ACUTE ATROPHY, SIMPLE ATROPHY, AND HYPERTROPHY OF THE LIVER.

THIERFELDER.

PHYSICAL DIAGNOSIS.

Preliminary Observations.

In the diagnosis of diseases of the liver, the safest course is to fix our attention first of all upon those appearances by means of which the physical peculiarities of the organ may be learned, for these peculiarities afford the most important starting-point for any conclusions respecting the anatomical condition of the liver. A correct idea of the position and volume of the liver can be obtained, under normal conditions, only by means of percussion. But not even this mode of examination will enable us to determine accurately the superior border of the organ (the situation of the vault of the diaphragm), for it is only quite gradually that the clear resonance of the right lung, below the line of the fourth rib, and upon the side of the thorax from the axilla downward, becomes duller. Upon the other hand, the dulness elicited in percussing from below upward, proceeding from that portion of the liver lying in close juxtaposition to the wall of the thorax, presents a sharp outline, which corresponds with the lower border of the right lung. This line of junction runs almost horizontally, curving but slightly upward, around the right half of the thorax, striking the right border of the sternum at its point of union with the sixth rib; the *linea papillaris*, or line extending perpendicularly downward from the right nipple, at the sixth intercostal space; the *linea axillaris* at the lower border of the seventh rib; and the *linea scapularis* at the ninth rib; reaching the spinal column at its point of union with the eleventh rib. It not unfrequently happens, that in thick-set individuals and those of short stature the upper line of dulness of the liver is situated higher by a single intercostal space than

is above indicated—a condition shown in any individual case to be normal by the fact that the heart's impulse is then felt in the fourth intercostal space. The superior line of dulness for that portion of the liver situated to the left of the right border of the sternum is indicated by a straight line drawn from the point where the line of dulness encounters the right border of the sternum to the seat of the heart's impulse. The line of dulness corresponding to the lower border of the liver is found most readily by percussing upon the abdomen upward toward the curvature of the ribs, pressing firmly with the finger or plessimeter—striking, however, but gently, or, if the abdominal parietes be thick, with but moderate force. The advantage of this procedure is this: that, in advancing from a locality resonant upon percussion to one of dulness, the boundary between the two regions is much more clearly determined than if we proceed in the opposite direction; and that it is only by means of the muffling effect of gentle percussion that the thin border of the liver is rendered appreciable above the loud tympanitic sound of the subjacent inflated intestine. It must be admitted, however, that, even when proceeding in the manner just indicated, we cannot always avoid bringing out a line of dulness situated somewhat above the margin of the liver, inasmuch as this is, for the extent of a finger's breadth, scarcely one centimetre thick. Whether the area of hepatic dulness is normal or not, as respects its extent and configuration, can be determined with less certainty from the measurement of its diameters than from the position and direction of its boundary-lines. According to the tables published by Frerichs,[1] the maximum and minimum of individual clinical measurements of the perpendicular diameter of the hepatic dulness vary commonly to so great an extent one from the other, that the figures indicating the mean measurement can hardly be accepted as normal.

A portion of Table V. upon page 40 is cited as an example; and there will be found appended to the average figures there recorded the minimum and maximum figures from which they are deduced.

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[1] Klinik der Leberkrankheiten. Bd. 1, S. 37–40. Braunschweig, 1858.

COMPARISON OF PERPENDICULAR MEASUREMENTS OF THE LIVER.

STATURE.	AXILLARY LINE.			MAMMARY LINE.			STERNAL LINE.		
	Min.	Max.	Average	Min.	Max.	Average	Min.	Max.	Average
From 67 to 100 ctms.									
Males	4.0	8.5	5.87	3.0	7.0	4.87	0.5	4.0	2.37
Females	2.5	7.0	4.36	1.5	7.0	3.94	1.0	5.0	3.28
From 100 to 150 ctms.									
Males	5.0	11.0	8.57	6.0	12.0	8.30	3.0	7.0	5.25
Females	6.0	13.0	9.04	6.0	12.0	8.64	3.0	9.0	5.74
From 150 to 160 ctms.									
Males	6.0	12.0	9.02	6.0	12.0	9.76	4.0	8.0	5.96
Females	6.0	11.0	9.09	7.0	11.0	9.10	4.5	7.0	5.77
From 160 to 170 ctms.									
Males	8.0	12.0	10.0	8.0	12.0	9.56	4.0	9.0	6.28

Bamberger found, upon the average, in thirty measurements made upon adults, that the extent of hepatic dulness in the axillary line was 12 ctms. in men, and 10½ ctms. in women; in the papillary line, 11 ctms. in men, 9 ctms. in women; in the parasternal line, 10 ctms. in men, 8½ ctms. in women; and the distance of the extreme left border from the ensiform cartilage, 7½ ctms. in men, 6½ ctms. in women.

A far greater uniformity and constancy is observed in the relations, as regards distance, between the lower border of the liver and the inferior margin of the thorax, than in the extent of the diameter above referred to and its relation to the stature. In the normal position and size of the organ, the lower border of dulness runs, as a rule, in such a direction that in the papillary line it is situated at the inferior margin of the ribs; in the axillary line, a little above the same; in the median line, nearly midway between the ensiform cartilage and the umbilicus, or somewhat nearer the former, and thence rises obliquely, with its left extremity terminating in the vicinity of the heart's impulse. In the space between the papillary and the median lines, it takes either an approximately horizontal direction, or else it begins here to curve somewhat upward. In the parasternal line the distance of the organ from the lower margin of the ribs is greater or less, according to their degree of curvature. Respecting the dimension of the left lobe, individual anomalies undoubtedly

occur frequently; the dulness produced by it often extends barely beyond the point of the ensiform cartilage, reaching not quite to the parasternal line, whereas at other times it projects far into the region between the left papillary and axillary lines. It is not uncommon in young children, even in the normal condition, for the lower limit of the area of dulness to extend in the papillary line beyond the lower margin of the ribs by one or two centimetres; and during the first year of life this is almost the rule. This irregularity is, moreover, occasionally observed in persons having a narrow thorax, when it should not be regarded as abnormal.

In morbid enlargement of the liver or of one of its two principal lobes, there results an extension of the dulness, commonly in a direction either downward, or downward and toward the left, attributable to the simultaneous increase in weight of the organ suspended from the diaphragm. The dulness extends in an upward direction when other contents of the abdominal cavity (meteorismus, fluid within the peritoneum, abdominal tumors) do not permit the downward enlargement; or when there exists a firm adhesion of the liver to the anterior abdominal wall; or when the enlargement is produced by tumors which bulge up above the convex surface of the organ.[1] The increase in the antero-posterior diameter of the liver causes a diminution of the tympanitic resonance in the lower part of the region of hepatic dulness, and increases the resistance appreciable upon percussion. Any *diminution* in the size of the liver always makes itself perceptible at the lower line of dulness. Since the left lobe is usually first affected, the left portion of this line is usually deflected at first upward and at the same time toward the median line, and subsequently, in the region of the right lobe, it approaches gradually nearer to the upper margin. This diminution in breadth and height of the area of dulness usually precedes the transformation of the dull sound into a tympanitic resonance, which spreads in the mass from below upward and

[1] In acute inflammatory enlargement of the liver it is commonly observed, according to *Sachs* (Ueber die Hepatitis der heissen Länder. Berlin, 1876. S. 38 f.), that there is developed first an enlargement in an upward direction, which subsequently, after the resistance from above has reached a certain degree, manifests a downward tendency.

from the left toward the right as the organ becomes more and more attenuated at the edges. Should, finally, the diameter of the right lobe become so small that the organ is no longer in contact with the anterior surface of the hypochondrium, there appears throughout the seat of the former hepatic dulness the clear tympanitic sound of the intestines, which take possession of the space rendered vacant by the wasting of the gland. In case of partial atrophy of the liver (syphilitic contraction), the vertical diameter of contiguous portions of the region of dulness may give very different measurements, in consequence of which the outline of the lower border may be very irregular.

In percussing the liver, but still more in the palpation of this organ, it is of great importance, if we wish to attain practical results, that everything should be avoided which may lead to erroneous conclusions, or which may complicate the examination. The latter should not be undertaken, therefore, upon a full stomach, for the percussion note being rendered dull in the vicinity of this organ, the determination of the boundary of the left lobe of the liver is made impossible; or, at other times, the stomach being distended by gas, this lobe may be dislodged upward. The precaution should also be taken of insuring previous evacuation of the bowels; fæcal accumulations in the right half of the colon may lie in such immediate relation to the liver as to be easily mistaken for a portion of that organ. It is an important requisite that the abdominal muscles should be as completely relaxed as possible during the examination; this will usually be attained if the patient lies with head and back resting upon a firm support, the thighs being moderately flexed at the hip-joint; whether, and to what extent, the entire upper part, or the head alone, should be somewhat raised, can be ascertained in individual cases by experiment. If the temperature of the examiner's hand is too low, or if pressure is applied too suddenly to the abdominal wall, troublesome reflex contractions of the muscles may be induced. Those parts which yield readily to pressure — such, for instance, as the free border of the liver when thin and movable, and the gall-bladder when filled and when the resistance of its walls is not altered—can be defined only by very careful palpation, if at all; but when stronger pal-

pation or deeper pressure with the ends of the fingers is necessary, this should always be done gently. It is only when a deep layer of ascitic fluid is situated between the abdominal wall and the anterior surface of the liver that the latter is, as a rule, more easily mapped out by means of a percussion-stroke of moderate firmness. In the course of the examination we should never fail to cause the patient to take a long breath. Sometimes it is only during the descent of the liver accompanying the act of inspiration, that this organ is rendered accessible to manipulation, at times to a considerable extent; moreover, it frequently gives an opportunity for observations that are valuable, especially in distinguishing the liver from neighboring organs that are the seat of morbid changes. Under certain circumstances, also, the position upon the left or right side, in so far as the lobes of the opposite side are then situated somewhat lower than they would be in the recumbent posture, may be essential in the palpation, especially with regard to that portion of the liver which is situated for the most part toward the right. The erect posture, as well as the knee-and-elbow position, never affords any advantage, but is much more apt to induce, owing to the stronger contraction of the anterior abdominal wall, a deadening of the percussion sound and an increased resistance at certain points, which may very readily lead to erroneous conclusions.

Under perfectly normal conditions nothing can, as a rule, be determined with respect to the liver from the sense of touch, inasmuch as this organ offers no greater resistance than that of the abdominal walls. When, however, the latter are unusually thin and relaxed, there may be at times detected beyond the right *rectus abdominalis* the border of the right lobe projected outward from beneath the arch of the ribs by the act of inspiration; and in the depression formed by the simultaneous separation of the two recti muscles may be distinguished still more plainly the corresponding position of the lower border of the left lobe, as well as a portion of the anterior and often also of the posterior surface of the latter. In the ordinary condition of the abdominal parietes the liver is, however, only to be felt when, in some portion accessible to palpation, its consistence is abnormally increased. In that case the problem is to acquire, by a proper

manipulation of this portion, a knowledge respecting its volume and mobility; the degree of its resistibility as a whole, and at certain points; the configuration and other peculiarities of its outer surface with reference to any inequalities, projections, and depressions. Attention should be directed particularly to the free margin of the accessible portion with respect to the above-mentioned conditions, and it should be observed whether it deviates from the normal direction of the inferior margin of the liver; whether it is rounded and thickened, or remarkably thin and sharp; whether the fissure for the gall-bladder can be distinguished; whether the bladder itself presents a smooth or uneven tumor; whether the *incisura interlobularis* occupies the median line, or is situated to one side of it; and whether any adhesions with other organs can be made out. If possible, the attempt should be made to force the fingers around the free edge, in order to reach the concave side of the liver, and to ascertain also the condition of its surface.

In cases where positive results are afforded by palpation, abnormal appearances are also observed very frequently in the region of the liver and its immediate vicinity. The enlargement of the organ may be so considerable as to induce decided distention, not only in the right hypochondrium and adjacent upper abdominal region, but also in the superjacent part of the right half of the chest, or in the entire lower portion of the thoracic cavity, and even in the entire abdomen. In higher degrees of enlargement the ribs are frequently tilted outward, the false ribs being forced over each other, and at the same time so rotated that their lower border becomes the anterior. Tumors that project beyond the outer surface of the liver frequently produce circumscribed swellings of the abdominal parietes or the false ribs. But even in cases where but slight increase in the volume and consistence of the organ is present, there may sometimes be detected upon the abdominal wall—provided its parietes be moderately thin—a shallow furrow, forced up and down by the act of inspiration, which serves to mark out the inferior border of the liver.

In exceptional cases only does auscultation contribute any material aid in establishing a diagnosis. In inflammatory alterations of the serous capsule there appears often at prominent parts

of the liver—as these move up and down during respiration, or as the abdominal wall is artificially moved over them by the physician—a friction sound like that of pleurisy, distinguishable by the hand or by means of the stethoscope.[1] In very rare cases, calculi within the gall-bladder, when brought into contact with each other, give rise to a sort of clinking. The line representing the boundary up to which the respiratory murmur of the left lung is audible, can never serve to determine the upper border of that portion of the liver in relation with the thoracic wall; this lies far below and at a variable distance from the latter.

Not all the deviations from the normal appearances that are revealed by a physical examination of the liver are to be accepted, without further investigation, as indications of morbid changes in the organ. The most frequent of these deviations attributable to varieties in the form and size of the liver have already been described. Other[2] changes, occurring quite independently, will be recognized in life, as such, at most only when other symptoms, which might point to a disease of the liver, are persistently absent. Changes in form, which, in view of their great frequency, and from the fact that, with very rare exceptions, they exert no appreciable influence upon the function of the gland, may be designated as acquired malformations, are produced in consequence of long-continued compression of the lower part of the thorax by tight articles of clothing, seldom, no doubt, simply by laced stays, but more frequently by tightly fastened coats and belts.

In slight grades of the so-called "tight-lace liver" only a shallow transverse furrow is observable upon the anterior surface of the right, and less often of the left lobe; and that portion of the liver situated below this depression, and which is not abnormally lengthened, is more easily moved forward and backward than under normal conditions. That portion of the hepatic peritoneum corresponding to the line of constriction is either unchanged, or it exhibits a slight milky opacity, which is most intense at the point of compression, and imperceptibly merges

[1] *Leopold* (Arch. d. Hlkde. Jahrg. 17, S. 395) observed, in the case of an enormously enlarged carcinomatous liver, loud blowing-sounds proceeding from the vessels, coincident in point of time with the arterial pulse.

[2] See *Frerichs* (loc. cit. S. 48 f.) for delineations of such changes.

above and below into the ordinary color of the liver at that part. Frequently the affected portion of the liver appears slightly granulated.

In case a long-continued or unusually severe pressure is exerted, then the modifications in form affecting the entire organ and the changes in texture at the point of constriction are more decided. That portion extending downward below the line of depression—the so-called tight-lace lobe—is attached to the principal mass of the organ only by a loose bridge of variable breadth, and often but a few centimetres thick, which is composed in part only of glandular substance; often in greater part, or even exclusively, of fibrous tissue. The tight-lace lobe seldom retains the normal form of the inferior segment of the liver, but is usually transformed into a roundish tumor, which presents upon its lower side no sharp border. It extends downward, to a greater or less distance, into the abdominal cavity, and admits of free motion forward and upward. At that part most exposed to constriction, the hepatic peritoneum is hypertrophied and indurated, and at times firmly attached by means of the perihepatic adhesions to the parietal fold. More frequently, however, this callosity is not attributable to circumscribed peritonitis, but is to be regarded simply as a result of the contraction of the gland, or as a *partial atrophy of the liver due to compression.* The connective tissue at this part is only relatively increased after the destruction of the hepatic parenchyma. In the indurated part may be seen, even with the naked eye, the outlines of vessels for the most part venous, and frequently, also, large gall-ducts and dilated lymph-vessels.

This callosity is composed of very firm connective tissue, tenacious, containing but few cells, and scantily furnished with capillaries; whereas the larger veins and single arterial branches supply the vascular communication between the tight-lace lobe and the liver. From this fibrous callosity are given out various broad cords of similar structure, that penetrate between the lobules and also between the lobular groups of the adjacent glandular tissue, as a result of which there is produced for a short distance from the surface the appearance of granulated liver;[1] moreover, the tight-lace lobe is often more richly supplied with connective tissue, and is firmer and dryer.

[1] Compare *A. Thierfelder's* Atlas d. pathol. Histologie. Taf. XVI. Fig. 1.

Of the peculiarities of the tight-lace liver we should bear in mind, with reference to the diagnosis: (1). The elongation of the organ, especially that of the right lobe, which may extend for a greater or less distance below the margin of the ribs, indeed even to the cæcal region. (2). The increased consistence of the constricted lobe, the result of textural changes of the parenchyma and the thickening of the capsule. (3). The tight-lace furrow, running in a horizontal direction, in the vicinity of which the liver may be so reduced by atrophy that folds of the intestine may arrange themselves above it, and, as a consequence of this, the area of dulness corresponding to the tight-lace lobe may appear cut off from that of the rest of the liver situated above, by a strip from which a clear tympanitic percussion-sound is emitted. (4). The mobility of the tight-lace lobe, which is at times so considerable that this part of the organ allows a free motion either forward or backward. Both the first-mentioned conditions are liable to lead to an incorrect diagnosis, in so far as the greater volume and firmer consistence of that portion of the liver adjacent to the abdominal parietes may also indicate serious disease of this organ; and the tight-lace lobe, which upon percussion appears to be detached, may easily be mistaken for another organ that has sustained morbid alterations. But the mobility of the tight-lace lobe and its displacement following the act of respiration, as well as the tight-lace depression, the existence of which can almost always be established, afford, as a rule, sufficient data for determining the true state of affairs. This solution will, moreover, be simplified by the fact that the changes in question are rarely encountered except in adults of the female sex; with whom, however, it should be added, the change may be said to be of quite common occurrence. The diagnosis is more difficult where, in exceptional instances, the upper third of the liver constitutes the seat of the constriction; this organ may then, as in a case reported by Frerichs (loc. cit., p. 52), occupy the entire upper half of the abdominal cavity, being not only appreciably elongated, but at the same time forced far over to the left. In the case quoted, the *ligamentum teres* was found at the cartilage of the eighth or ninth rib upon the left side.

The determination of the volume of the liver is not unfrequently embarrassed by pathological alterations of the adjacent organs. In case the diaphragm be forced downward by any abnormal contents of the pleura or of the pericardium, or by tumors of the mediastinum, then the liver is brought into more extensive relation with the abdominal parietes, which results in lowering either wholly or in part its inferior border of dulness.[1] Although, under such circumstances, there almost always results, in consequence of the disturbance in the circulation attributable to the diseased condition of the thoracic organs, an actual increase in the volume of the liver, the extension of the dulness downward is, nevertheless, to a greater or less extent, due to the consecutive dislocation of the organ in this direction. And that such a displacement really exists, may usually be readily recognized when it is brought about by pulmonary emphysema, pneumothorax, extensive pericardial exudations and tumors of the mediastinum, there being no difficulty in these disorders in detecting also the corresponding depression of the superior line of hepatic dulness. The determination of this line is not possible, however, in extensive pleuritic effusions on the right side, because the percussion note over this exudation throughout the affected half of the thorax is quite as dull as over the adjacent liver. It often happens that inspection will suffice to prevent our falling into the error of referring this dulness in its entire height to the hypertrophied liver; for an obliteration of the intercostal spaces, such as is produced by pleuritic exudations, does not occur as the result of diffused enlargement of the liver; whereas, on the one hand, the hypertrophy may lead to rotation of the ribs, pleuritic exudations, on the contrary, can never produce this effect. But the other methods of physical examination furnish also, as a rule, data for the differential diagnosis. In case the dulness which extends abnormally high up over the thorax is due to a uniform enlargement of the liver, then its superior boundary runs in a horizontal direction from the sternum to the spinal column, and the apex of the heart is also situated at

[1] Extreme deformities of the thorax, the result of rachitis, by reducing the capacity of the chest and depressing the diaphragm, may produce a similar effect.

an abnormally high point corresponding to the elevation of the diaphragm. Upon the other hand, the dulness characteristic of pleuritic exudations is bounded generally by a line which ascends in a direction from before and within outward and backward; and if the right lobe of the liver is pushed considerably downward and toward the median line by this exudation, as the *ligamentum suspensorium* acts as the fulcrum of the liver, the left lobe may become raised, and in consequence of this the apex of the heart may, no doubt, also assume an abnormally high position; but, as a result of the simultaneous displacement of the mediastinum, it is always dislocated to a like or even greater extent outward toward the left. In those rare instances where the superior boundary of dulness of a pleuritic exudation maintains a uniform height throughout the entire extent of the right half of the thorax, and is, moreover, unchanged when the patient is recumbent, then, as a consequence of the existing adhesion between both pleuritic surfaces in the vicinity of the effusion, this line does not move downward upon deep inspiration; whereas, at the superior boundary of dulness, occasioned by the upward encroachment of the liver, the respiratory displacement may, as a rule, be plainly perceived. This latter movement is absent from the superior line of hepatic dulness only in those exceptional instances where the pleuritic surfaces in the vicinity have become adherent, or when—as is no doubt of not uncommon occurrence—the diaphragm, having been forced high up into the thorax by a tumor of the liver, has become inactive from atrophy of its muscular tissue. Such a tumor, however (echinococcus, carcinoma, hepatic abscess), never produces a dulness extending at a uniform height around the entire right half of the thorax, but only a circumscribed area of dulness, the margin of which curves convexly above that of the rest of the liver. It should be observed, however, that precisely similar appearances are sometimes produced by the dulness caused by cystic exudations in the lower part of the right pleura; and the discrimination between these and the hepatic tumors is the more difficult from the fact that there occurs also in the latter a diminution of the vocal fremitus, obliteration of the intercostal spaces, and a sensation of fluctuation. Under such circumstances the result of an exploratory

puncture alone will, at times, determine with certainty the diagnosis.

The liver may also be displaced downward by peritonitic exudations between the diaphragm and the convex surfaces of this organ, in consequence of which the hepatic dulness extends in a proportionate degree downward; and, moreover, these exudations may, by their presence, produce dulness in that part from which they have expelled the liver. In these cases—which, upon the whole, are very rare—it is not always possible to avoid confounding the exudation with enlargement of the liver; the diagnosis will be the most readily determined when the exudation is very extensive, or when, as in several of the cases described by Bamberger, gas is also present, for then the appearances are quite similar to those produced by an encysted exudation at the base of the lung, or by a pneumothorax at this point.

It occasionally happens that the appearance of an increase in the bulk of the liver is produced by tumors of other abdominal organs lying in such immediate proximity that the dulness proceeding from them is directly continuous with that of the liver. This occurs in tumors of the stomach, retroperitoneal lymph-glands, pancreas, transverse colon, the great and lesser omentum, and the right kidney. In a portion of these cases, however, we can plainly distinguish, by means of the fingers, and usually also with the eyes, the free edge of the liver—which, indeed, in consequence of its displacement by the tumor, often deviates more or less from its usual position,—as well as its mobility upon respiration. In many cases, however, the tumor is in such intimate contact with the liver that the boundary between the two cannot be defined by the most careful palpation. Here, when the tumor is so immovable as to prevent the liver from descending with the act of respiration, this absence of the respiratory displacement will usually afford a sure indication of the presence of a foreign tumor, rather than of a portion of a diseased liver projecting low downward, for even when such a morbid liver extends upon both sides even to the inguinal region, the downward movement of its inferior border accompanying deep respiration is usually perceptible. The influence of respiration upon the position of the organ is absent, apart from the case above

mentioned, only when the contractility of the diaphragm is impaired by the great encroachment of the liver upon the cavity of the thorax; or when, in extreme lateral hypertrophy, the liver presses against both hypochondria—conditions under which a simulated hypertrophy of the liver, resulting from the presence of a tumor situated immediately below it, would scarcely be suspected. If, on the other hand, an adjacent tumor, whose outlines cannot be distinguished from those of the liver, partakes of the respiratory movement of that organ, the two forming one continuous mass similar in form to an enlarged liver, then an error will be unavoidable unless functional symptoms or anamnestic signs should assist to a correct diagnosis.

Errors of an opposite character respecting the volume of the liver arise much more frequently from the extensive relations of the abdominal viscera containing air; the organ appears smaller than it really is, because a portion of its anterior surface is covered by a fold of the intestines, or because it has been forced upward and backward by the inflated or displaced bowel. The former phenomenon occurs, in rare cases it is true, as a physiological condition when the transverse colon occupies an abnormal position between the liver and the border of the ribs; more frequently it is an accompaniment of morbid changes in the organ (diminished resistibility of the parenchyma, formation of furrows on the anterior surface), or of dilatation of the lower aperture of the thorax resulting from ascitic distention of the abdomen. This condition can commonly be recognized, upon careful percussion, by the deviations in the line of the inferior margin of dulness. The line corresponding to these deviations—when, for example, the *flexura coli dextra* has pushed itself forward—suddenly rises abruptly for several centimetres in the vicinity of the axillary line, subsequently reassuming an almost horizontal course, or sooner or later descending in the form of a bow. Moreover, the loop of the intestine thus superposed may often be so firmly compressed that the influence of the liver in deadening the resonance upon percussion can be distinguished. If a portion of a decidedly hypertrophied liver is covered by folds of the intestine, the organ can usually be detected upon palpation, when the intestines are either pushed aside or compressed; for

in such cases the consistence of the organ is also usually abnormally increased. In displacements by inflated bowels, the liver, as a rule,[1] is forced upward and simultaneously backward; and the latter dislocation may be so extensive that the intestinal loops may lie in contact with the entire portion of the anterior thoracic wall subjacent to the lower border of the lungs and the heart. The hepatic dulness diminishes also in its perpendicular diameter as a result of the elevation of its inferior boundary, and may ultimately entirely disappear, in consequence of which the pulmonary resonance upon the right side in front, and occasionally also even upon the side of the chest, borders immediately upon that of the intestine. The most frequent cause of such a dislocation is intestinal meteorismus and a diminution in the capacity of the abdomen, resulting from the presence of fluids in the peritoneal cavity, or from tumors, especially those which project upward from the pelvis. The recognition of the immediate cause of the diminished hepatic dulness is, in such cases, easy; but to determine accurately the size of the liver is, on the other hand, impossible; and if the theory of atrophy is rendered probable upon other grounds, no results of any examination made while the bowel is thus inflated or forced upward can serve to confirm such an opinion.

Finally, it must not be overlooked that, in individuals with relaxed abdominal parietes, meteorismus may occur without apparently distending the abdomen; and that, under these circumstances, the diaphragm is all the more forcibly pushed upward, while the hepatic dulness is in a proportionate degree diminished. Here, however, the position of the inferior border of the lungs and of the apex of the heart, as well as the cardiac dulness, afford sufficient data for a correct diagnosis.

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[1] In exceptional cases the displacement may occur more toward the side against the right concavity of the diaphragm, provided the colon, in consequence of constriction or compression of the lower part of the bowel, is disproportionately distended. *Frerichs* (loc. cit., p. 66) narrates several cases of this sort.

Floating Liver.

Hepar migrans.—Fegato ambulante.

Under the above head is designated a more or less perceptible downward dislocation of the liver, the cause of which cannot be attributed to a pressure exerted upon the organ from above, such as has just been described (p. 43). The first example of this kind was reported by Cantani in 1866, since which time eight other cases have been published.[1]

A. Cantani, Ann. univers. di Medic. 1866. Nov. p. 373. Schmidt's Jahrbb. Bd. 141. S. 108.—*R. Piatelli*, Riv. clin. VII. 8. p. 239. 1868. Schmidt's Jahrbb. Bd. 141. S. 112.—*E. A. Meissner*, Schmidt's Jahrbb. Bd. 141. S. 107. 1869.—*G. Barbarotta*, Il Morgagni, XII. p. 848. 1870. Schmidt's Jahrbb. Bd. 149. S. 170.—*F. N. Winkler*, Arch. f. Gynäkol. Bd. 4. S. 145. 1872.—*Fr. Vogelsang*, Memorabilien. Jahrg. 17. 1872. Nr. 2. S. 67.—*G. Leopold*, Arch. f. Gynäkol. Bd. 7. S. 152. 1874.—*W. Sutugin*, Arch. f. Gynäkol. Bd. 8. S. 531. 1875.—*Chvostek*, Wiener medic. Presse. 1876. Nr. 26–29.

Although in none of these nine cases has the diagnosis as yet been confirmed by autopsy, nevertheless in seven there can be scarcely any doubt as to the existence of the alleged change in position, though the two remaining examples (Piatelli, Vogelsang) are not quite so clear.

All these observations, without exception, were made in women[2] who had borne children; the ages at which the abnormal position of the organ first became perceptible were, respectively, 29, 37, 39, 41, 42, 43, 50 (about), 53, 54 years. Some of these women belonged to the lower, others to the so-called "better" orders.

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[1] A case reported by *Salomone-Marino* has not been included in this account, because the original report (Rivista clin. di Bologna, 1874. Maggio) was not accessible to me, and the abstract of the same in the Jahresbericht of *Virchow* and *Hirsch*, for 1874, Bd. 2, S. 257, contains merely the following statement: "In *Federici's* clinique at Palermo *Salomone-Marino* observed a woman, twenty-six years of age, with a tumor situated in the lower half of the abdomen, which careful examination, aided by the anamnestic signs, etc., demonstrated to be the liver hypertrophied and prolapsed, though in other respects normal, whereas the spleen was found in the right hypochondrium. The thoracic organs occupied their normal position."

[2] According to *Wassiljew* (Petersb. med. Wochenschr. 1876. No. 30; review in Centralbl. f. d. med. Wissensch. 1876. S. 873) the movable liver occurs also in men.

Three of them were accustomed to lace tightly; with regard to the others it is merely stated that they had worn laced stays; Sutugin states distinctly that his patient had never laced tightly. The symptoms indicating the existence of floating liver made their appearance in the cases of Cantani, Meissner, and Winkler, several weeks after confinement at full term; in the case of Barbarotta, where the woman had previously borne six children, several months after an abortion accompanied by profuse metrorrhagia; in Vogelsang's case, that of a woman who had borne three children, in one year after the menopause; in Leopold's case, seven years after the last (seventh) confinement; finally, in each of two cases but one confinement had occurred, between which and the appearance of the dislocation of the liver an interval of ten years had elapsed in Sutugin's case, and at least twenty-three years in that of Piatelli, and here this lesion came on during the course of some abdominal disorder, probably chronic peritonitis. With Sutugin's patient a second pregnancy terminated in abortion in the third month in consequence of a fall, but no record is given of the time at which the displacement occurred. In Winkler's case the symptoms of floating liver appeared after a heavy weight had been lifted. As regards the physical condition of these women at the time of the development of the dislocation of the liver, by most of the writers no history is given: the patient of Leopold was poorly nourished, very thin, and emaciated; that of Sutugin was fleshy, but somewhat anæmic. In at least one-half the cases (Barbarotta, Winkler, Leopold, Sutugin) there was a relaxed, pendulous abdomen, and in two instances mention is made of the extraordinary thinness of the abdominal parietes; Vogelsang describes, moreover, the outward projection of the entire abdomen, and Cantani the tenderness of the abdominal muscles; in Piatelli's cases, however, the abdomen was prominent in the middle and somewhat above, and the superficial integument could be pinched up in thick folds.

From this comparison of those conditions which might perhaps be considered as etiological factors, it is obvious that to no one of them, with the exception of sex, can any decided influence be ascribed in producing the lesion of floating liver. This affec-

tion occurs exclusively in women, as is the case also with floating spleen; but while, in the spleen, the cause of the lengthening of the ligaments is due to a long-continued traction exerted upon them by the organ whose weight has been increased in consequence of morbid enlargement, no analogous cause is to be found for the extension of the hepatic ligaments, since in all cases yet reported, with one exception (Barbarotta), the depressed liver appears to present the normal volume and consistence. The circumstance that the women in whom a floating liver was observed had all borne children, led to the attempt to refer the origin of the dislocation to certain processes resulting from pregnancy. Cantani thought that the uterus when advanced in pregnancy tends to produce a backward pressure upon the liver, and thereby traction and extension of its ligaments; but Meissner had previously pointed out the improbability of this hypothesis, maintaining that a pressure exerted against the inferior surface of the liver must simply push the organ upward against the diaphragm; and if it were really powerful enough to produce the dislodgment, as assumed by Cantani, symptoms of disturbance of the biliary secretion and of the circulation, as well as of nutrition and the function of the liver, would scarcely fail to supervene; whereas in no case of floating liver has the occurrence of such symptoms in a previous pregnancy been remarked. It should, moreover, be added that the *fundus uteri*, even at the end of the ninth month, does not reach up to, or at most barely touches, the liver, provided the size and position of this organ is normal; and even this can only take place in case of anteversion, which condition appears to have been present in half of the above cases, as indicated by the relaxed pendulous abdomen remaining. Winkler, in his attempt to explain the pathology of floating liver, attached the greatest importance to a pendulous abdomen produced by pregnancy. According to this author, it is chiefly by means of the intra-abdominal pressure that the liver is maintained in its normal position, and any considerable diminution of this pressure, which, in accordance with his theory, follows the relaxation of the abdominal walls, must induce a depression of the diaphragm and the liver. This theory is shown, however, to be untenable, because, as has been justly

maintained by Leopold, a depression of the diaphragm has not been observed by any writer, with the exception of Winkler, and the occurrence of a depressed liver is extremely rare, as compared with that of a pendulous abdomen, which is so common. But the extremely rare occurrence of the former must always present serious obstacles to all attempts at explanation based upon the idea of demonstrating any direct relation between dislocation of the liver and pregnancy. Any such theory is, at all events, rendered extremely improbable by the circumstance that, in some cases, during a series of years previous to the appearance of the floating liver no further pregnancy had taken place. Some authors have suspected that too tight lacing might be the cause of the falling of the liver; but this theory is contradicted by daily experience, which shows that, as a rule, this pernicious custom is much more likely to give rise to alteration in the form of the organ rather than to changes of its position. Moreover, if this theory were correct, the disproportion between the frequency of the cause and of the effect would be very conspicuous. So long, then, as pathological anatomy fails to furnish us with any adequate explanation, we are compelled, in accordance with the theory proposed by Meissner, and adopted by Leopold and Sutugin, to regard an abnormal length of the suspensory ligaments of the liver—meso-hepar, as Meissner designates it—as a congenital anomaly. When this predisposition is present, a variety of causes may give rise to a falling of the liver; great relaxation of the abdominal parietes, severe physical labor, possibly, also, excessively tight lacing appear to have served as the causative agents in the cases above presented.

In all of these seven cases in which a correct diagnosis appears to have been made, the *symptoms* described as characteristic of floating liver perfectly coincide with each other. While the hepatic dulness was wanting in its normal situation, the full, tympanitic percussion-sound of the intestines succeeding immediately the clear, non-tympanitic sound of the right lung, there was detected in the middle or inferior abdominal region, occupying chiefly the right side, and extending toward the left slightly beyond the median line, a tumor which in its physical

peculiarities resembled the liver, and which admitted of being forced into the position normally occupied by that organ.

Independently of the general similarity in point of volume and configuration, the identity of the tumor with the liver was confirmed by the broad curvature of the surface directed upward, and especially by the peculiar character of its inferior margin. The border, in the cases accurately reported, was thin or sharp—Sutugin alone reported it as flattened,—while more frequently (Cantani, Meissner, Leopold, Sutugin, Chvostek) a superficial fissure could be detected, corresponding in its position to the *fossa interlobularis* or the *fossa cystis felleæ*. In the cases of Cantani and Leopold, the dull percussion-sound over the tumor changed gradually, toward the inferior border, into a tympanitic resonance. Moreover, in several of the cases above reported, careful palpation revealed certain other characteristic conditions. Winkler, by pressing the hand between the arch of the ribs and the tumor, detected the *ligamentum suspensorium* as a tightly stretched, thin membrane; whereas to Sutugin it resembled a band running from above to the middle of the tumor. Winkler succeeded in touching the greater portion of the inferior surface, and recognized therein distinct furrows; he could not detect, however, the gall-bladder, which was not to be distinguished from a portion of the intestine. Leopold, on the other hand, observed behind the inferior border a small tumor suggestive of the gall-bladder. The superficial surface of the tumor felt smooth, its consistence, as a rule, being that of the normal liver. In the case of Barbarotta alone, the small lobe was of a stony hardness, the large lobe being also somewhat indurated—presumably in consequence of interstitial hepatitis, as the patient had experienced fever for several months.

The distance of the liver from its original position varied with the different cases. In Winkler's patients the true superior boundary of the organ in the *linea papillaris* was demonstrated by percussion to lie beneath the sixth rib, and the inferior border six ctms. below the arch of the ribs. In Leopold's case the hepatic dulness began at a point a finger's breadth above the inferior margin of the thorax, and extended as far as the hori-

zontal ramus of the os pubis. In the remaining cases the organ had descended altogether from the right hypochondriac region, its superior edge being found at a greater or less distance below the arch of the ribs. The liver appears to have reached the lowest point in Cantani's patient, for it here lay entirely below the umbilicus, and in the erect posture its lower edge was concealed behind the os pubis. While the length of time during which the dislocation had existed before coming under medical observation is, no doubt, not without influence, yet this fact alone cannot be held responsible for the degree of displacement; for in Meissner's case, when the trouble had not, according to all appearances, existed longer than in that of Winkler (*i. e.*, about two months), it was so considerable that the liver reached down to within two fingers' breadths of the symphysis pubis.

The locality occupied by the displaced organ lay always directly beneath that in which it is found in the normal condition; and, consequently, it was bounded upon the right by the prolongation of the right *linea axillaris*, while toward the left it extended but a few centimetres (1 plessimetre, Cantani; 4 ctms., Sutugin; 6½ ctms., Winkler) below the median line. In its new location, moreover, the organ always lay, upon the whole, crosswise; yet the descent had not always taken place to a similar degree throughout the whole breadth of the organ; in Winkler's case, the left lobe, and in that of Leopold the right, was somewhat the lower.

The dislocated liver manifested constantly an abnormal mobility. When the patient lay upon her side, the organ descended toward the inclined side, as was observed in several cases by the women themselves (Cantani, Barbarotta). By these lateral movements the organ was made to describe the figure of a circular arch, having its convexity directed downward, whose size was proportionate to the degree of descent, and whose radius seemed to have its central extremity at times in the right hypochondrium, at others at the point where the left lobe is in relation with the diaphragm. It is asserted by Piatelli alone that the organ alternately fell and rose upon respiration. All the writers, however (with the exception of Vogelsang, whose account is in this respect deficient), emphasize the great mobility

in an upward direction. In five cases it was found possible, without difficulty, at times after the hips had been somewhat elevated, to restore the liver completely to its usual position, which then emitted the dull percussion-sound, just as in the normal condition. In Sutugin's case there remained also, after the replacement, between the hepatic dulness and the pulmonary resonance, a tympanitic zone of a finger's breadth. In Chvostek's case the superior edge of the organ did not ascend above the seventh rib; and in that of Piatelli the tumor could be pushed upward only so far that its superior edge stood directly beneath the lower margin of the ribs.

The abnormal position of the liver was almost always associated with morbid subjective symptoms. In one case only (Vogelsang) was there freedom from pain, while the enlargement of the lower abdomen, in a woman who had not previously menstruated for the period of a year, occasioned no further embarrassment than that arising from apprehensions as to the existence of pregnancy. In three cases there was present a feeling of weight, hardness, and fulness of the abdomen, in consequence of which Meissner's patient was prevented from stooping over; while Cantani's was so overcome by the dread of having some serious disorder, that she relapsed into a condition of hysteria and religious melancholia. Piatelli's patient—who came under observation for the first time thirteen years after the origin of the dislocation—had previously experienced the sensation of hardness and weight at a higher part of the body. In the remaining four cases there was violent pain. Barbarotta's patient complained of violent twinges in the right side, shooting up to the shoulder and neck. Chvostek's patient suffered continuously from gastralgic and dyspeptic disorders. In two other cases the pain was excited chiefly by any violent movements of the head (Leopold, Sutugin); and the same peculiarity was noticed in the case observed by Winkler, where, moreover, the pains were aggravated by bending backward, as well as by the attempt to push the tumor downward or toward the left, whereas relief was afforded by bending forward and by supporting the body with the hands. The case of Winkler proves, however, that the descent of the liver may also give rise to still other phe-

nomena; the patient alluded to, upon raising a heavy weight, experienced not only cutting pains in the right hypochondrium, most violent when reclining upon the left side, but also frequent eructations, nausea, cold sweats, and an anxious expression—a combination of symptoms that continued during three days; one year and a half later, after an unusually severe fatigue from washing, she was again attacked by these pains, which were then supplemented by the development of a moderate icterus lasting four weeks. The origin of the icterus, and of the severe pain—which at times bore a close resemblance to the colic of gall-stones—was referred quite correctly by Winkler to the formation of a loop or twist in the *ductus choledochus* and the other cords so abundantly supplied with nerves, which communicate with the hilus of the liver. This explanation would seem plausible in the other cases, also, where the pain was located in the vicinity of the tumor; whereas, respecting the pain shooting up to the shoulder, of which Barbarotta's patient complained, the theory of traction exerted upon the duplicature of the peritoneum reflected between the diaphragm and the liver, is more probable.

None of the above writers, with the exception of Winkler, allude to the existence of icterus; nor is any mention made of disturbances in the functions of the stomach or intestines. Furthermore, notwithstanding the long-continued existence of the displacement, there may be an absence of all morbid symptoms except the subjective troubles above described. Cantani's patient, who had been the subject of a floating liver for eleven years, appeared well-nourished, with a well-developed muscular system, an elastic, white skin, and a natural redness of the cheeks and external mucous membranes; her hysteria disappeared as soon as the apprehensions as to the nature of her tumor were allayed. The case reported by Piatelli terminated indeed fatally, under symptoms of anarsaca, a short time subsequent to the examination revealing the abnormal position of the liver (no necropsy was made, Piatelli not having been informed in season of the death); but this case was complicated with chronic peritonitis.

The symptoms upon which the *diagnosis* of floating liver is

based are the following: 1. In the middle or inferior abdominal region, and for the most part in the right half, is found a tumor which corresponds in its physical properties with the liver. 2. The superior edge of this tumor is separated from the inferior border of the right lung by a zone, emitting a clear, tympanitic sound, which extends from the anterior surface of the body around to the right side of the chest. 3. The tumor admits of complete restoration to the normal position of the liver. The great importance of the third symptom, as regards the differential diagnosis, is illustrated in the case reported by P. Mueller.[1] In this woman, a tumor, situated in the vicinity of the umbilicus, was mistaken for a floating liver, from the circumstance that it presented all the physical properties of the liver, even the fissure in the sharp inferior edge corresponding to the *incisura interlobularis;* while in the region normally occupied by the liver there was no dulness whatever. At the autopsy, however, the tumor proved to be the omentum considerably thickened in consequence of chronic inflammation; whereas the liver, reduced in size by one-half, and firmly adherent to the diaphragm, lay in the posterior portion of the right hypochondrium, covered by folds of the small intestine and the stomach. If in this case the attempt had been made to push the supposed dislocated liver into the position naturally occupied by the organ, the failure to accomplish this—the hypertrophied omentum was adherent to the transverse colon—would have indicated the improbability of the diagnosis. Moreover, the fact that, in the case of Vogelsang—which, it must be admitted, is on the whole rather superficially described—no mention is made of the possibility of replacing the tumor, while, in Piatelli's case, this replacement could be but imperfectly accomplished, appears, as has been already remarked, to have left the diagnosis but insufficiently established. In the latter instance, where there existed simultaneously chronic peritonitis, it must indeed be admitted that the descended liver may have been limited in its mobility in consequence of adhesions to other abdominal organs; yet, in the light of Mueller's experience, the existence of peritonitis tends to suggest doubt as to

[1] Deutsches Archiv f. klin. Med. Bd. 14, S. 146.

the diagnosis. In Mueller's case, moreover, the tumor resembling the liver presented also, in another respect, a condition differing from that of floating liver; it extended in a transverse direction from the right to the left *linea mamillaris*. It is thus obvious that the theory of floating liver is fully established only when the tumor in question occupies, with the greatest portion of its volume, the right half of the abdomen.

Therapeutically, the application of a broad, firm abdominal support has proved to a certain extent beneficial, as in four cases the subjective pain was thereby either allayed or considerably alleviated. In the patients of Meissner and Winkler, the liver was held back *en masse* by means of a similar binder, so that, when standing, the anterior border of the organ extended but a little (at the most two inches, Meissner; barely a few centimetres, Winkler) below the lower margin of the ribs. Winkler's patient, who wore the support eleven months, and then discarded it, continued free from pain for a still longer period; only after six months did the pain recur, as the result of severe labor; she then resumed the binder, and consequently continued in perfect health for the two years following.

Hyperæmia of the Liver.

Etiology.

The division of the various forms of hyperæmia of the liver into those produced by some impediment to the discharge of the blood, and those originating in an increased afflux, does not admit of being strictly adhered to. There are, indeed, numerous cases, in the origin of which, as may be readily observed, the latter agency is alone operative; and again others in which the nature of the more remote cause necessitates the adoption of the theory of dilatation of the affluent vessels; but there remain, still, many others in which it is most probable that both increased determination and obstruction simultaneously share in the production of the hyperæmia.

Taking, therefore, the conditions as presented to the observation of the physician, the following causes may be distinguished:

Different Forms of Obstruction to the Circulation.—Whatsoever interferes with the outflow from the hepatic veins into the inferior *vena cava* tends to produce obstruction of the blood in the liver. In quite exceptional cases this may be induced by constriction of the branches themselves of the hepatic veins, in consequence of chronic *periphlebitis hepatica* (*vide* Diseases of the Hepatic Veins). Somewhat more frequently the obstruction has its origin in a narrowing of the *vena cava* above the junction of the hepatic veins, produced by tumors in this region (aortic aneurisms, carcinomatous tumors of the retroperitoneal glands), as well as by extensive exudations in the left pleural cavity. As has been demonstrated by Bartels,[1] the latter may push the mediastinum so forcibly toward the right, that the *vena cava* at the *foramen quadrilaterum* is bent almost to a right angle, which, as has been shown by Roser,[2] serves to account for the circumstance that severe forms of hyperæmia of the liver occur oftener by far in empyema of the left side than of the right.

But much the most frequent cause of arrest of the circulation in the hepatic veins is the increase of the lateral pressure in the inferior *vena cava*, in consequence of that functional incompetence of the right side of the heart which is wont to supervene in a variety of serious affections of the respiratory organs and heart. These affections are: congenital atelectasis; pneumonia; diffused bronchitis; general pulmonary emphysema; extensive atrophy of the lungs; long-continued compression of large portions of the lungs by kyphoscoliosis; pleuritic exudations; intrathoracic tumors (especially aortic aneurisms and large mediastinal tumors); furthermore, the different lesions of the cardiac valves,[3]—above all, the incompetence of the tricuspid valve, and stenosis

[1] Deutsches Arch. f. klin. Med. Bd. 4, S. 265.

[2] Archiv f. Heilkunde. Bd. 6, S. 40.

[3] According to the observations of *A. Steffen* (Jahrb. f. Kinderheilk. Bd. 5, S. 55), enlargements of the liver consecutive upon hyperæmia arising from obstruction of the circulation of the blood, particularly in incompetence of the mitral valve, are of rare occurrence in childhood; whereas, according to other authors—*B. Gerhardt* (Lehrb. d. Kinderkrankh. 2. Aufl. S. 214)—the relation existing between enlargement of the liver and valvular affections in the case of children is precisely the same as in adults, in whom, moreover, a mitral insufficiency well compensated for exerts no influence upon the liver.

of the left auriculo-ventricular opening,—as well as inflammatory and degenerative alterations of the cardiac muscle and moderate pericarditic exudations. When, in the above-named affections, no hypertrophy whatever of the walls of the dilated right ventricle is produced, or when this hypertrophy does not attain that degree necessary for the disposal of the increased contents, or when—as is more generally the case—it becomes, at a more advanced stage, insufficient, there is then produced an engorgement of the entire venous system of the body, in which, at the outset, the venous vessels of the liver forming a part of that system are implicated.

To mechanical obstruction is also to be referred that form of hyperæmia of the liver designated by many writers as atonic, which makes its appearance in the later stage of wasting diseases and in senile marasmus. Here, in consequence of the poor nutrition, as perhaps also of the imperfect innervation of the muscles of the heart, the action of the latter is enfeebled, so that the passage of the blood from the veins into the arteries is impeded. The immediate cause of the over-distention of the liver with blood, under these circumstances, is not the diminution of force with which the blood flows into the organ, but the reduction of the quantity in which it is taken up by the heart.

Unfavorable Influences of a Dietetic Character.—During digestion, in consequence of the afflux toward the gastro-intestinal mucous membrane and the diffusion of fluids in its capillaries, the blood flows through the portal vein to the liver more rapidly and in greater quantity than usual. In persons who eat too much or too frequently, this periodic hyperæmia of the organ may assume gradually a permanent character, though fluctuating perhaps in intensity. If we attempt to ascribe the origin of this permanent congestion to the simple fact that the over-distention of the affluent vessels has continued for too long a time, and has been too frequently repeated, we must, nevertheless, admit that the immediate cause is a dilatation of these vessels combined with hypertrophy of their walls, corresponding in extent to their increased contents (active dilatation). But no one has as yet demonstrated such a condition at the roots of the portal vein referable to the influences under consideration, and the question-

able hypothesis may, for the present, be the more readily dismissed, since, as a rule, other better-authenticated data are offered for the explanation of the development of chronic hyperæmia of the liver arising from immoderate eating. In the greater number of individuals the disproportion between the absorption of nutritive material and its waste is ascribable chiefly to their sedentary mode of life, and, above all, to their relative muscular inactivity. Since, as is well known, respiration is more superficial in the sitting posture than when standing or even lying down, and since in health deep inspirations are produced almost exclusively by more active movements of the body, it will be understood that, under the conditions above named, we lose an important agent in the propulsion of the current in the hepatic veins; the blood, conducted in larger quantity to the liver, flows off more slowly, and the ultimate subdivision of its vascular system, the capillary network, becomes engorged. In the same manner—that is to say, by a restriction of the free action of the respiratory movements—still other conditions commonly tend, in these cases, to produce hyperæmia of the liver: such, for instance, as the distention of the stomach by a large quantity of ingesta; the accumulation of fæces and gas in the intestinal canal[1] not unfrequently met with; and the corpulence so frequently developed in consequence of over-eating, which, through the increase in the volume of the abdominal contents, and especially of the abdominal walls, impedes the downward flattening of the diaphragm. But, on the other hand, corpulence can, moreover, give rise to stagnation of blood in the liver: when, for instance, an excessive deposit of fat in the sub-epicardial connective tissue results in a reduction in the thickness of the muscular

[1] The theory adopted by *Frerichs*, that the extensive formation of gas and accumulation of fæcal matter within the intestinal canal, by forcing the blood from the roots of the portal vein against its trunk and the liver, may give rise to temporary hyperæmia of this organ, would seem to be improbable. A pressure exerted upon the wall of the intestine strong enough to cause a contraction of its veins must inevitably induce, in a still higher degree, a diminution in the calibre of its capillaries; the increase of the obstruction in the latter thereby produced reduces the quantity of the affluent blood and the rapidity of its current; consequently less blood finds its way into the veins of the intestine, and that, too, with diminished force, while the flow of blood to the portal vein must thus be lessened.

substance of the heart, and especially of the right ventricle, there then results, in proportion as the pro-expulsive power is diminished, in the place of an increased flow to the liver, an impediment to its escape.

High living tends to produce a morbid hyperæmia of the liver, and all the more readily if articles of food are used which act like acrid matters either upon the gastro-intestinal mucous membrane or upon the liver itself. Under this class of substances may be enumerated the irritative spices, such as mustard, pepper (black, as well as the Spanish pepper used in the tropics); furthermore, strong coffee (on account of its empyreumatic oil); and, notably, alcohol. With respect to the latter, we know that, even in the reduced form in which it is commonly found in the stronger spirituous liquors employed as a beverage, it tends to produce hyperæmia of the mucous membrane of the stomach, which serves to render highly probable the theory of its direct influence upon the liver. This theory has, however, its most powerful support in the inflammatory alterations which the liver undergoes in consequence of the immoderate consumption of strong liquors. The fact that, by means of this agent alone, an abnormal increase in the quantity of blood in the organ is produced, has not as yet been demonstrated by autopsies either in human beings where death occurred while in an intoxicated state, nor in animals into whose stomachs relatively large doses of alcohol had been experimentally introduced.[1] The theory derives, however, a certain support from the fact that, in the case of pre-existing hyperæmia of the liver, over-indulgence in alcohol tends, as a general rule, to aggravate the symptoms.

Traumatic Influences.—After contusion or severe concussion of the liver (from pressure, or from a blow inflicted in the neighborhood of the liver, in consequence of a fall from a considerable height), there sometimes appear symptoms pointing to hyperæmia of the gland. Although these symptoms may often be due to sub-serous or deep-seated rupture of the parenchyma, yet their rapid disappearance renders it, in other cases, quite prob-

[1] Of twenty-one dogs on which *P. Ruge* (Virchow's Archiv. Bd. 49, S. 252) instituted experiments in the manner above indicated, relating to the effect of alcohol, in five alone did the liver appear more or less congested.

able that their origin is to be referred to a paralytic dilatation of the hepatic vessels, produced possibly by mechanical irritation of the organ, in the same way as the relaxation of the vessels of the intestines and mesenterium occurs in the experiments of Goltz, made by tapping upon the abdomen of a frog.

Atmospheric Influences, Infectious Diseases, etc.—It is a very prevalent idea that a continuously high atmospheric temperature may entail congestion of the liver. So far as concerns the temperate zone, however, this theory can hardly be accepted; evidence is wanting, at least, that hyperæmia of the liver is of more frequent occurrence during the warm season than at other times. The gastric and intestinal catarrhs, so prevalent during the summer and early autumn, may, indeed, give rise to catarrhal icterus, but they do not tend to produce over-distention of the gland; and even in the tropical regions it appears doubtful whether any direct influence is exerted by the climate upon the quantity of blood contained in the organ. The theory that this quantity is augmented in Europeans who have emigrated to the tropics has appeared tenable, partly in view of the results of autopsies, and partly from the circumstance that, according to the reports of Annesley, Twining,[1] and others, an increase of the biliary secretion appears as an almost constant effect of a change of climate, and this increased secretion would favor the assumption of a more abundant flow of blood to the gland. But the fact of this superabundance of bile is itself very questionable, for its existence has been by no means confirmed by the presence of symptoms regarded as characteristic of this condition, such as yellow tinge of the skin, bilious vomiting, stools of a bilious character, excessive distention of the gall-bladder.[2] As regards, furthermore, the circumstance that in tropical regions an abnormal congestion of the liver forms a post-mortem appear-

[1] *Vide Hirsch*, Handbuch der histor.-geograph. Pathol. Bd. 2, S. 307 ff.

[2] *Morehead* (Clinical Researches on Diseases in India. London, 1856) pronounces the alleged increase in the activity of the liver, resulting from a high temperature, a fable. Compare, also, *Schwalbe* (Klima und Krankheiten der Republik Costarica. Deutsch. Arch. f. klin. Med. Bd. 15), according to whose representation (pp. 145 and 325) the biliary secretion is not only not augmented during the early portion of a sojourn in the tropics, but, upon the contrary, is diminished.

ance of remarkable frequency, this is to be referred chiefly to the participation of the organ in the miasmatic diseases which prevail endemically in most of these regions. In the malarial fever of the tropics the liver is not unfrequently engorged with blood quite as fully as the spleen. In tropical dysentery the organ appears frequently, in recent cases, hyperæmic; and the acute form of tropical hepatitis begins, as a rule, with a general hyperæmia of this gland. That there is here presented a complication produced by a warm climate is not probable. Hyperæmic swelling of the liver occurs as a symptom of intermittent fever in the temperate zones also; and in two other diseases, as we shall see later (*vide* Suppurative Hepatitis), its presence can scarcely be otherwise explained than upon the theory of a special miasma producing its effect upon the liver, or by an irritation of the liver from unfavorable dietetic influences.

Among the remaining infectious diseases in which anatomical investigation reveals more or less constantly an augmentation of the supply of blood contained in the liver, although during life symptoms pointing to such a congestion are much less frequently observed, may be enumerated bilious typhoid, spotted typhus, scarlet fever, cholera, epidemic cerebro-spinal meningitis, and charbon [anthrax; splenic fever].

In scurvy, also, the liver displays, for the most part, considerable plethora, although, according to the experience of Frerichs, the opposite condition is at times met with. In diabetes mellitus, also, the liver is in many cases engorged with blood.

It is only in the disease last mentioned that paralysis of the vaso-motor nerves can be said to constitute probably the immediate cause of the hyperæmia; for, as is well known, hepatic congestion is also developed by puncture, as in the experiments of Bernard. But, on the other hand, in all the other diseases herein referred to, it is thus far quite undecided whether the dilatation of the hepatic vessels arises in consequence of a disturbance of the innervation or of the nutrition of their walls.

Suppression of Habitual Hemorrhages.—There are often manifested at the menstrual epoch symptoms of hepatic congestion, occurring either in place of the uterine flow or immediately preceding it, or after it has ceased sooner or more abruptly than

usual. Here there occurs, manifestly, a determination of blood to the liver, which, it is extremely probable, is connected with the excitation of the ovarian nerves referable to the maturing ovum, induced by a reflex mechanism like that involved in the afflux to the genital organs. We cannot always in such cases demonstrate the presence of influences which, as is shown by experience, may tend to produce disturbance in the latter organs, such as sudden chills, violent mental emotions, etc.; and even when such influences are present, it remains almost always inexplicable why the reflex process, which in the genital organs is either not at all or only to a slight extent operative, is transferred directly to the liver. Equally obscure is the mode of origin of those forms of hepatic congestion which occasionally make their appearance during the climacteric years, and afford evidence of their etiological relation to the menopause, not only by their simultaneous occurrence, but also by the circumstance that they temporarily disappear, or at least become modified, as often as menstruation again recurs.

The cessation of hemorrhoidal discharges of blood that have become habitual is also thought to be followed, under certain conditions, by congestion of the liver. As a rule, however, this variety of hyperæmia arises from other pre-existing causes (obstructions in the lesser circulation, dietetic disturbances), and only becomes more prominent from the circumstance that it is aggravated by the interruption of the discharge from the rectum, which serves to regulate the degree of pressure in the portal system.

Other Varieties of Diseases of the Liver.—The theory that a large majority of all structural changes and new-growths are preceded by a congestive condition of the organ, or certain portions of it, is by no means in accord with the results of either clinical or pathologico-anatomical experience. Even the inflammatory processes do not invariably begin with an hyperæmic stage, while with respect to the pseudo-plasmata, those only, as a rule, that are characterized by a very rapid growth induce a collateral or—but far less frequently, no doubt—irritative hyperæmia of the surrounding parenchyma. Induration of one of the lobes of the liver, or obliteration of those branches of the portal

vein with which the lobe is supplied, occasionally gives rise through collateral fluxion of blood to apoplexy of the other lobe (Frerichs).

Hyperæmia of the liver, so far as it makes its appearance as the symptom or sequel of other affections, is etiologically related to these diseases: thus in individuals of all ages there may occur hyperæmia due to mechanical obstruction of the blood and also to infectious diseases. As regards the idiopathic variety peculiar to hot climates, the reader is referred to the etiology of Suppurative Hepatitis. The congestion induced by dietetic irregularities is decidedly peculiar to middle life. But in the production of this latter form of congestion, besides the dietetic influences, there is involved, at least in many cases, another factor—viz., an especial predisposition on the part of the patient. Of different individuals who indulge freely in nutritious diet and irritative articles of food, leading at the same time an inactive or sedentary life, some become the subject of hepatic congestion, obstruction, hemorrhoids, etc., while others remain free from these disorders. The cause of this dissimilarity can at present be only surmised; possibly it is to be referred to the condition of the walls of the vessels belonging to the portal system, the existence of very considerable individual differences in this respect having been demonstrated in the arteries.[1] It is possible, also, that the development, nutrition, and innervation of the muscular tissue of the intestine may exercise a material influence. According to my own experience at least, the injurious sequelæ of intemperance seem to occur much oftener in gourmands and immoderate drinkers of a constipated habit than in those of the opposite tendency. The predisposition to habitual hepatic congestion, here under consideration, is often inherited, and may then appear in the same families for several generations. It must obviously be admitted that there may exist a similar predisposition toward a menstrual hyperæmia of the liver. A somewhat analogous condition is suggested also in that form of hyperæmia due to obstruction; in certain affections, for instance, it is not always the liver, but frequently the kidneys or the

[1] *Virchow*, Ueber die Chlorose. Berlin, 1872. S. 2, 8, 13 ff.

mucous membrane of the digestive apparatus, that constitute the organ in which the results of over-distention of the entire venous system first of all and most distinctly appear; and with reference, moreover, to the degree of the alterations in the liver, the separate cases present varieties which are by no means invariably proportionate to the extent of the obstructions to the circulation; in consequence of which, as is stated by Botkin,[1] the susceptibility of the liver to the effects of an increased venous pressure cannot be the same in all individuals.

Anatomical Changes.

Congestive hyperæmias of the liver, which involve equally the whole organ, are observed in the cadaver in extremely rare cases only, if at all. From the marked apoplexy of certain portions of the liver, where their temporary position or the direction of the larger vascular branches does not favor the free outflow of the blood, we are, however, often enabled to form an opinion during the life of the patient as to the increase in the quantity of blood throughout the entire organ—at least in all cases where etiological agencies are present sufficient to account for the congestive hyperæmia (increased functional activity of the organ after the ingestion of certain substances, or specific irritative agents; higher temperature in acute febrile affections; initiatory stage of inflammatory processes in the liver itself). The liver is in such cases hypertrophied, softened, and generally of a dark red color, while upon section the surfaces at the affected part are uniformly covered with blood. Smaller portions of the organ, for instance, the parts in the immediate vicinity of abscesses, new-growths, parasites, etc., present frequently the picture of congestive hyperæmia; indeed, in such cases a mechanical obstruction of the blood may also, no doubt, often be present, which tends to favor the production of the over-distention.

Of much deeper significance is the hyperæmia of the liver due to obstruction, which also gives rise, at the outset, to an increase

[1] Medicin. Klinik. 1. Heft. Berlin, 1867. S. 72 f.

in the volume and to greater softness of the organ. Inasmuch as there are in exceptional cases mechanical causes which tend to produce this derangement (compare chapter on Etiology), and inasmuch as in the greater number of cases these causes persist for a long time, or at least frequently recur, it results that this form of mechanical hyperæmia is generally lasting and leads to permanent structural changes in this organ. The hepatic vein forms the solitary channel for the outflow of blood from the liver, and in the ramifications of this vein—the central veins—as well as in its roots, the capillaries occupying the central portion of the acini, we encounter, therefore, first of all, and in many cases exclusively, the following condition of obstruction of the blood: the central veins and the capillaries opening directly into them are found to be distended, the adjacent glandular cells being atrophied often to a considerable extent under the pressure of the dilated vessels. Brownish or even black pigment alone is left behind, forming usually the final remains of the parenchyma cells embedded in the connective tissue around the central veins. Whether proliferation of the connective tissue actually takes place at that point, or whether, after the wasting of the hepatic cells, only a relatively larger quantity of this tissue is present in the central portion, must in individual cases often remain undetermined, since both conditions seem to occur. Although in many instances the atrophy extends far toward the periphery of the acini, thereby resulting in a considerable diminution in the secretory glandular substance, yet it rarely amounts to a complete disappearance of entire acini. The liver is throughout diminished in size, dark brown, and of a firm consistence. Upon section, it is more resistent than normal; at the divided surfaces it is dark brownish-red, exhibiting small acini, numerous largely dilated central veins being visible to the naked eye; from the surfaces of sections made in a transverse direction, dark drops of blood often ooze out; the surrounding tissue is discolored black. This represents the ordinary picture of the typical so-called *cyanotic atrophy of the liver*. A modification of these appearances is not unfrequently due to the fact that, especially in the earlier stages of the process, where dilatation of the hepatic veins and dark red discoloration of the central

portion of the lobules is already present, the portal zone of the acini exhibits large accumulations of fat in the hepatic cells. There is thereby produced a peculiar mottled or marbleized appearance, which has been designated by the term *nutmeg liver*.

It will be readily understood that under certain conditions, not to be considered at this point—where, for example, the peripheral portions of the acini are occasionally deprived of blood, or contain large masses of fat, while the central portions retain their normal quantity of blood—a similar picture may also be produced from the contrast in color likewise present. It is not advisable, however, to term this condition also nutmeg liver; the genuine nutmeg liver implies the existence of an abnormally dark discoloration of the centre of the lobules produced by stagnation of the blood.

There is frequently added to the above-described central atrophy of the substance of the liver, as has been demonstrated by Liebermeister, an increased development of the interstitial connective tissue, which at times appears only in streaks, while at others it affects more uniformly the entire organ, and is attended by a corresponding increase in its consistence—*cyanotic induration*. While this process is going on at the expense of the glandular parenchyma, and produces, owing to the consecutive shrivelling up of the newly-formed tissue, a diminution in the volume of the liver, there results an atrophy of the glands often quite extensive, and a condition which presents very great similarity to genuine cirrhosis, and which was formerly frequently confounded with that affection. There is by no means, however, any lack of distinguishing signs; the surface of the cyanotic indurated liver is indeed granulated, but the granulated spots are in part more superficial, in part smaller and of less regular form, than in cirrhosis. The cut surfaces are also of a darker hue, the stagnation being usually long continued. Altogether, the alterations appear to be less uniformly developed, and the aspect of the entire organ presents, therefore, as a rule, nothing so characteristic as in the case of fully-developed cirrhosis. Even in this stage of the affection the remains of the hepatic parenchyma not unfrequently contain, independently of the dark pigmentation about the central veins above described, considerable fat and likewise greenish bile-pigment. In this way

the liver may present a very peculiar variegated picture, which, like the entire process resembling cirrhosis, has been designated by the term *atrophied nutmeg liver*.

Symptoms.

The hyperæmic swelling of the liver is at times to be recognized only by percussion: the extensive area of dulness involves, as a rule, both lobes in like degree. The increased volume may, however, often be made out also by palpation. That portion of the organ projecting beneath the arch of the ribs gives rise either to merely an increased resistance of the epigastrium and of the right hypochondrium, or it presents, as far as the inferior edge—which may be readily felt, and which commonly appears somewhat less sharp and firm than normal—an elastic smooth surface. It is only in higher grades of stagnation, and in rare traumatic cases, that the tumefaction becomes so considerable that the hepatic region is perceptibly distended. In cardiac affections the enlarged organ may project downward by a hand's breadth and more, beyond the margin of the ribs. The hyperæmic tumor of the liver is characterized by the fact that it can increase, and subsequently diminish, in size more rapidly than is the case in any enlargement of the gland induced by other causes. Thus, in affections of the heart and lungs there may be frequently seen, during an attack of violent dyspnœa, a remarkable increase in the volume of the liver, and, upon the other hand, after copious venesection, a perceptible diminution. The swelling of the organ arising from immoderate eating exhibits not unfrequently, after hemorrhoidal discharges of blood, a rapid decrease. In a patient suffering from intermittent fever I observed, in three consecutive paroxysms, that upon each occasion the perpendicular diameter of the hepatic dulness was greater by one-and-a-half to two centimetres than during the interval of the apyrexia. A gradual, but persistent, diminution in the size of the liver swollen from stagnation of the blood, makes its appearance when the stage of atrophy and induration supervenes; while the superior margin of dulness remains unaltered, the lower boundary is moved more and more upward toward the arch of the ribs, receding at times,

according to Liebermeister, from two to three fingers' breadths within a few weeks. Upon that portion of the anterior surface of the liver then adjacent to the abdominal parietes the granulations, resembling minute uneven points, may occasionally be felt.

The increased volume of the liver generally makes itself known to the patient through a *feeling of fulness or tension* in the right hypochondrium, which is aggravated by strong movements of respiration and by external pressure. It is only when the hyperæmia which has been slowly developed continues moderate, that no abnormal symptoms are, as a rule, experienced; but even then the portion of the gland not covered by the ribs is wont to be sensitive to pressure. If, on the other hand, the tumefaction is rapidly developed, as in the acute cases occurring in warm climates, and frequently in traumatic and in menstrual hyperæmia, or if it experiences a rapid augmentation, as after the indulgence in rich or irritating articles of food, then it may be associated with severe pain in the hepatic region embarrassing the breathing and making it difficult to lie upon the right side, and occasionally with pain in the right shoulder. Should a very considerable increase in size gradually supervene in consequence of long-continued obstruction of the circulation, then lying upon the left side may sometimes induce an aggravation of the subjective disturbances.

Icterus frequently supervenes in the higher grades of nutmeg-liver in individuals subject to heart-disease, and produces, in conjunction with cyanosis, that peculiar, almost greenish, discoloration of the face which is almost characteristic of such patients during the last stage. It is observed comparatively seldom, however, when the stagnation of blood in the liver is dependent upon chronic pulmonary diseases. Notwithstanding this striking and as yet inexplicable diversity exhibited by the venous hyperæmia of the liver as regards icterus—this difference being proportionate to the remoteness of the causé—the phenomenon is, nevertheless, to be regarded as most probably a symptom of this hyperæmia, and to be attributed to the resorption of the bile. This hypothesis derives its principal support from the accumulation of the biliary pigment in more or less numer-

ous hepatic cells observed always at the post-mortem examinations of such cases. Under these circumstances, then, we may at times demonstrate anatomically the existence of an impediment to the outflow of the secretion due to the contraction in the calibre of some intra-hepatic biliary ducts from catarrhal tumefaction, originating in the extension of the stagnation to the veins of the mucous membrane of these canals. Finally, it may be unhesitatingly assumed that acini, swollen by hyperæmia, and the distended lesser ramifications of the portal vein[1] may exert a compression upon the interlobular biliary ducts in which, when cyanotic induration is present, even the shrivelled-up connective tissue may also take part. It may be added that the biliary obstruction dependent upon stasis of blood in the liver is invariably restricted to a part of the organ, as is shown by the fact that only a portion of the parenchyma cells exhibit the biliary discoloration; while the corresponding icteric symptoms are also of slight intensity. The yellow hue is confined principally to the conjunctiva and the skin of the upper half of the body; in the lower part it is, as a rule, absent, this being, almost without exception, œdematous in the cases under consideration; the fæces do not present the peculiar character indicative of the absence of bile; the quantity of biliary pigment to be detected in the urine is slight. In the other varieties of hyperæmia of the liver, apart from bilious typhoid, icterus is but rarely met with, and usually in a still more insignificant degree. In the idiopathic form (the first stage of hepatitis) of hot climates it is found, according to the calculations of Rouis,[2] in about four per cent. of the cases. The habitual over-distention of the liver with blood which occurs in immoderate eaters and drinkers, and occasionally in women at the climacteric period, is frequently associated with a yellowish tinge of the conjunctiva; this is, however, not always of an icteric character, but is due frequently

[1] *Icterus neonatorum* must apparently be also referred to a compression of the biliary ducts from distended blood-vessels in those cases where it makes its appearance as a concomitant of atelectasis or inflammatory affections of the lungs. Compare *F. Weber*, Beitr. z. pathol. Anat. der Neugeborenen, Heft 3, S. 55; and *E. Neumann*, Arch. d. Heilk., Bd. 9, S. 45 f.

[2] Rech. sur les suppurations endém. du foie. Paris, 1860, p. 118.

to a slight hyperæmia of the loose subconjunctival connective tissue between the corners of the eyes and the margin of the cornea, as well as to the presence of numerous fat-cells in this tissue.

According to Senator's theory as to the mode of origin of "menstrual jaundice" in the four cases observed by him,[1] there may be developed, in place of the menstrual hemorrhage, or when this discharge is abnormally scanty, an hepatic hyperæmia characterized by the circumstance that it is followed constantly or to a remarkable extent by icterus. When in these cases an hepatic hyperæmia really exists,[2] this is, in all probability, attributable to the increased determination of blood from the hepatic arteries; while the striking frequency of the icterus is to be explained by the fact that, primarily, the mucous membrane of the biliary ducts and the interstitial connective tissue, and, secondarily, the secreting tissue, have been affected by the blood-engorgement, whereby a narrowing of the excretory canals, consecutive upon the catarrh and compression, might readily be induced.

A higher degree of icterus in hepatic hyperæmia is referable either to the catarrhal obliteration of the intestinal portion of the *ductus choledochus*, or to the obstruction of the latter or of the *ductus cysticus* by concrements.

Gastric symptoms may be observed in very many cases. The affection of the stomach and intestine to which these are due is not, however, a result of hepatic hyperæmia, but is induced by the same cause as the latter disorder. In this way, in the above-mentioned diseases of the respiratory and circulatory organs, the extension of the mechanical obstruction from the hepatic veins to the portal vein and its roots gives rise to venous hyperæmia of the walls of the digestive tract, indicated by symptoms of disturbed digestion and retarded peristaltic action, and occasionally also by tumefaction of the hemorrhoidal veins. These symptoms are frequently associated with those of hepatic hyperæmia

[1] Berl. klin. Wochenschr. 1872. Nr. 51.

[2] In the third case reported by *Senator*, in which gastric disorders were present, the dejecta colored a clayish gray hue, and the presence of biliary acids, plainly demonstrable in the urine, point rather to an icterus occasioned by duodenal catarrh.

in gourmands and topers, derangements in the nutritive function being induced, sooner or later, by the daily repeated irritation of the mucous membrane (and possibly the muscular tissue) of the *primæ viæ*. Moreover, in the various infectious diseases enumerated in the etiology there appears usually, in addition to the hepatic hyperæmia, an affection of the digestive organs, which, however, is related to the former only in so far as both constitute the concomitant effects of the action of the infecting material.

Disorders of the intellect, characterized by depression or hypochondriasis, not unfrequently appear in patients suffering from chronic hepatic hyperæmia; yet, in accordance with our psychiatrical experience, it is much more probable that this derangement is caused by the co-existing gastro-intestinal catarrh than by the affection of the liver.

Ascites accompanies, indeed, very frequently the severe varieties of hyperæmia resulting from obstruction of the circulation; it is, however, for the most part, an accompaniment of general dropsy, which is wont regularly to supervene in the later stages of the cardiac and pulmonary affections that give rise to the stagnation. It is only where the obstruction has given rise to atrophy and induration of the liver that it takes an active part in the production of ascites. The contracted connective tissue exerts a pressure upon the various ramifications of the portal vein, by means of which the impediment to the flow of blood in the roots of this vessel dependent upon the general disturbance in the circulation is further aggravated. In addition, also, to those causes of the serous transudation in the abdominal cavity referable to the heart or lung, there exists still another influence located in the liver itself. Inasmuch as the development of connective tissue in the liver always precedes any decided obstruction in the general venous system of the body, the ascites always makes its appearance in such cases after that of the œdema of the lower extremities, and is often associated with general dropsy; it is developed sooner, however, than would be the case if it were due simply to the general obstruction, and attains a considerable degree when it corresponds to the stage of dropsical effusion in other organs. Agencies by means of which the latter variety of ascites is materially diminished or temporarily allevi-

ated (such as the action of digitalis, the diminution of a bronchitis, etc.), exert upon the former no influence, or at least a much less decided effect. Bamberger long ago maintained that this prominence of ascites, as compared with the other dropsical symptoms, is characteristic of nutmeg-liver in general, while by Liebermeister it was more definitely pronounced indicative of cyanotic induration of the liver—theories since confirmed by Niemeyer, Koehler, Cantani, and others. It is, indeed, true that this phenomenon is not in every instance sufficiently well marked. Where a very considerable general dropsy already exists, it may occasionally be no longer possible to determine whether or not the ascites present has a special source of origin within the portal venous system, apart from its dependence upon the general stagnation of the blood. Although the cyanotic stagnation of the liver necessarily produces also an increase of the over-distention in the splenic vein, yet no enlargement of the spleen can, as a rule, be detected. Liebermeister, who first of all pointed out this striking fact, endeavors to explain it upon the theory that, under the influence of the extensive hyperæmia of the spleen, as also of the liver, a development of connective tissue takes place tending to the production of atrophy.

Course, Duration, Mode of Termination, Prognosis.

Whether the hyperæmia exists in acute, or, as is more frequently the case, in chronic form, depends upon the character of the cause; and its duration is likewise determined by the persistence of the causal agencies. After contusions of the organ, the symptoms usually make their appearance at once, and often subside within a very short time, but occasionally only after some weeks. In affections of the heart and lungs the symptoms are developed, for the most part, gradually, and may persist for a long time. They then manifest more frequently, however, fluctuations in their intensity, according as the degree of incompetence of the right ventricle increases or diminishes, which depends partly upon the amount of impediment to the circulation present in the heart or in the pulmonic circulation,

partly upon the conditions of nutrition or innervation of the heart, and partly upon the total quantity of blood contained in the system. A similar relation is observed in hepatic congestion due to immoderate eating and irritative articles of food, the symptoms of which are not unfrequently aggravated after each meal or after indulgence in alcoholic liquors; and, upon the other hand, diminish when, in consequence of more frequent evacuations from the bowels, or hemorrhage from the vessels of the rectum, the excessive tension in the venous portal system is relaxed. When the trouble is due to a disturbance in the menstrual function, the attacks occasionally recur for several months in regular rhythm.

Strictly speaking, the affair can terminate in one of two ways: the abnormal engorgement either subsides with the removal of the cause, or, if this cause is persistent, it continues until death. There is, indeed, a possibility, at least in hyperæmia resulting in obstruction to the circulation, of a transformation into some other form of disease, which may also in turn disappear, without leaving behind any appreciable alterations in the organ; as is shown, for example, in the rapid restoration to the normal condition after the evacuation of pleuritic exudations. But when the cause of the obstruction is not removed until after a large number of hepatic cells have been already destroyed by the excessive distention of the roots of the hepatic veins, then the gland itself may shrivel up so as to fall below the normal volume. If development of the interstitial connective tissue should supervene in consequence of long-continued obstruction, then the atrophied nutmeg-liver acquires a certain independence, in so far as the ascites depending upon it continues present, whereas the other symptoms of dropsy disappear. Of the other varieties of hepatic hyperæmia, it is not known that they can induce derangements in the nutrition of the organ. When this appears to be the case, these disturbances have their origin in the same cause as the hyperæmia; and the latter is the first effect of an influence which, when continuing for a long time or recurring frequently, manifests its effects upon the interstitial tissue or the hepatic cells (abuse of alcoholic liquors, gluttony); or it forms a link in the chain of those alterations which

the liver experiences in inflammatory or neoplastic processes (*hepatitis suppurativa*, carcinoma, etc.).

The *prognosis* depends entirely upon the conditions constituting the cause; the hepatic hyperæmia does not of itself involve danger to life. When, however, this lesion is long-continued, or frequently recurs, it will very properly lead to an unfavorable prognostication, inasmuch as it is then wont to be the precursor or concomitant of other incurable affections of the organ, such as cirrhosis, carcinoma, etc. The atrophy of the liver produced by obstruction may finally induce also, by its after-effects, an acceleration of the fatal termination of chronic affections of the heart and lungs.

Diagnosis.

Inasmucn as the symptoms above considered may be observed in other affections of the liver, and even in diseases in which this organ takes no part whatever, we are justified, therefore, in assuming the existence of hepatic hyperæmia only when at the same time the presence of one of the causative agencies above described can be demonstrated. In the case of hyperæmia arising from mechanical obstruction of the blood, this is, as a rule, easy; because these affections which give rise to the stoppage of the circulation afford almost always direct physical signs, and induce, likewise, symptoms of obstruction in the other portions of the venous system of the body. The cyanotic induration of the liver may be distinguishable by the disproportion between the ascites and anasarca, even when the diminution in the volume of the organ cannot be kept under observation, or, owing to the ascites, cannot be established with certainty. Means of distinguishing it from genuine cirrhosis of the liver—which appears, moreover, to occur only in extremely rare cases in those affections of the heart and lungs that give rise to obstruction (Liebermeister) — are afforded by the series of after-effects among which the dropsical symptoms make their appearance—in case of cirrhosis, first, ascites; in case of atrophied nutmeg-liver, first, œdema of the lower extremities,—and by the conduct of the spleen, this organ exhibiting, as a rule, in nutmeg-liver,

a normal volume, but being, on the other hand, in cirrhosis commonly enlarged. In the other forms of hepatic hyperæmia the diagnosis is often more difficult and more uncertain, not only from the circumstance that the symptoms are at times not well marked, but, even where they are distinctly developed, it not unfrequently remains doubtful whether they are to be attributed to simple plethora of the organ, or whether they may not be due rather to more radical changes in the gland which are referable to the same exciting cause, and which run their course accompanied by the same manifestations, such as hemorrhages, deposits of adipose tissue, interstitial and suppurative inflammation, etc. The course of the affection will here afford the principal guide to a decision, inasmuch as the symptoms, in so far as they are connected with hyperæmia, either completely subside, or, at least, manifest those fluctuations already described, which are to be referred to the variable intensity of the etiological factors and other agencies tending to produce congestion of the hepatic vessels.

Treatment.

The treatment should, from the outset, be directed as far as possible toward the causative agencies; and this indication becomes all the more imperative when the hyperæmia of the liver is developed gradually, or when there is a recurrence of the attacks. In congestion arising from an immoderate indulgence in varied food, associated with insufficient muscular activity, the most important requisite consists in a suitable change in the diet and habits of life. In recent cases such a change is usually sufficient to dispel the disease; and where this improvement is not brought about until after the administration of certain remedies (to be presently enumerated), directed especially to the hyperæmia, the abandonment of these pernicious dietetic habits forms the sole prophylactic against a recurrence of the disease. The diet should be reduced to the quantity appropriate to the individual case, taking care to avoid such articles of food as are rich in fat, highly seasoned, difficult of digestion, and tending to produce flatulence; also alcoholic liquors and strong coffee. The most

suitable diet will consist, as a rule, of lean meat, eggs, white bread, tender vegetables, and acid fruits; whereas milk and articles of pastry, such as are recommended by many, are not admissible, at least not in all of those cases where there exists a great tendency to the formation of fat. With the view of accelerating the hepatic circulation and stimulating the metamorphosis of tissue within the body, the patient should be directed, furthermore, to alternately stand and sit while at work; he should frequently draw voluntarily a long breath; should indulge in walking, riding, and other gymnastic exercise in the open air; and should likewise drink freely of water or simple acid beverages. When, after the subsidence of the hepatic hyperæmia, the problem is how to prevent its recurrence, a very moderate indulgence in the lighter spirituous drinks may, at the most, be permitted.

If the hepatic hyperæmia is dependent upon the suppression of the menstrual functions, then the attempt may be made to establish or restore the hemorrhagic discharge from the genital organs by means of warm foot, or hip baths, or full baths, the uterine douche, or the application of leeches to the vaginal portion of the uterus. The baths are especially appropriate when it is desired to prevent a recurrence of the menstrual afflux to the liver, while venesection is preferable for allaying such a determination already established.

The form of hepatic hyperæmia arising from mechanical obstruction may often be permanently relieved by an appropriate treatment of the affection constituting the primary cause of the derangement (as in capillary bronchitis and pleuritic exudation), but is far more frequently only temporarily allayed or modified (as in cardiac affections and emphysema); in cases of the latter class the improvement follows most frequently the timely exhibition of digitalis.

If it should prove impracticable to fulfil these causal indications, or should these measures prove insufficient, it will next be advisable to attempt to reduce in a more or less direct manner the quantity of blood in the liver, an end best attained in numerous cases by the administration of cathartics. While the action of these drugs tends, by accelerating the peristaltic motion, to restrict the resorption from the intestine into

the blood, and, in a measure, even to attract water into the intestine, the over-distention of numerous roots of the portal vein is reduced, which necessarily causes a diminution of the lateral pressure throughout the entire portal system. This treatment is, of course, especially appropriate when an abnormally increased determination of blood proceeding from the intestine forms an essential element in producing the derangement of the liver. On this account, in chronic hyperæmia of the liver arising from the indulgence in rich or irritating articles of food, the most important remedial agent, apart from an appropriate and abstemious diet, consists in a course of treatment at such springs as Karlsbad, Marienbad, Tarasp, Franzensbad, Elster, Kissingen, Homburg, and others. In selecting a particular mineral water, we should be guided principally by the constitution of the patient. Springs rich in Glauber's salt and carbonate of soda are appropriate for corpulent, robust individuals, to whom may also be recommended a short course of the genuine bitter waters (Friedrichshaller, Saidschützer, Ofener). The herb-, grape-, and whey-cures are at times quite as beneficial as the mineral springs, but are inferior to the latter not only in the certainty of their effects, but also from the fact that they are more apt to interfere with the digestive functions. When it becomes necessary to suspend the administration of the remedies above alluded to, owing to the season of the year or other conditions, or because the result of the treatment has proved unsatisfactory, then the preparations of rhubarb, buckthorn bark, aloes, and the like may be resorted to, with which may be combined the so-called resolvent extracts, and at times the sulphates and tartrates of the alkalies. The laxative agents may also be of benefit in all other varieties of hyperæmia of the liver not dependent upon increased afflux from the portal vein, whenever they tend, in the way above described, to lessen the blood-pressure in the ramifications of this vessel, and thereby in the entire hepatic capillary system. In the acute congestion, the neutral salts in large doses are especially serviceable, on account of their prompt action. In hyperæmia arising from obstruction, the milder vegetable aperients deserve, as a rule, the preference, because they admit of long-continued use. Under proper restrictions, the employment of soda- and saline-waters,

containing Glauber's salt, is by no means contraindicated; decided relief is indeed not seldom afforded by the use of these agents, when, in the course of chronic cardiac affections, and before the appearance of the dropsical stage, the symptoms proceeding from the liver constitute the prominent feature. The above-named springs prove efficacious, likewise, in tumors remaining behind after intermittent fevers.

With the view of reducing the plethora of the organ by means of an increased metamorphosis of the ingredients of the blood contained in the hepatic cells, remedies have also been administered to which have been ascribed the effect of stimulating the flow of the biliary secretion. Calomel has, until quite recently, occupied a prominent position among these remedies; but since its cholagogue action has been shown to be more than improbable, it should now be resorted to in the treatment of hyperæmia of the liver only when in any particular case other indications render it preferable to other laxatives. Resin of podophyllum is believed by American, English, and Belgian physicians to have the effect of expelling the bile, and on that account has been regarded by many as a cathartic especially suitable in hepatic accumulations; whether it actually possesses this property is as yet not fully settled. We do know for a certainty, however, that by the increased absorption of water by the blood of the portal vein the biliary secretion is increased; to which circumstance may also be attributed, in part, the benefit to be derived from drinking water, and from a course at certain mineral springs. Among the mineral waters to be recommended in cases of chronic hepatic hyperæmia should be included the sulphur springs; these exert, as a rule, no laxative influence to which their beneficial effect can be referred;[1] according to the hypothesis of Roth,[2] the sulphuretted hydrogen, when diffused into the blood of the portal vein, favors the restoration of the old red blood-corpuscles by combining with the iron contained in them, whereby an increased amount of material for the formation of the bile is obtained. The treatment by means of sulphur

[1] *J. Braun*, Lehrb. der Balneotherapie. 3. Aufl. Berlin, 1873. S. 483.

[2] Bad Weilbach und sein kaltes Schwefelwasser. Wiesbaden, 1855. S. 15.

waters is especially indicated in hyperæmia of the liver arising from an excess of blood in the portal vein. Recoveries attributable to the employment of these waters have also been reported in cases where the disease was the result of intermittent fever or of menstrual derangements.[1]

Local abstractions of blood are indicated in severe acute cases and in the exacerbations of chronic hyperæmia. As a rule, the application of leeches in the immediate vicinity of the anus forms the most appropriate procedure, since through the anastomosis of the hemorrhoidal veins with the cutaneous veins of the neighborhood, on the one hand, and with the hemorrhoidal branch of the inferior mesenteric vein, on the other, the quantity of blood in the portal vein is most readily reduced. Undoubtedly, leeches and cupping-glasses applied in the vicinity of the liver produce an effect on the quantity of blood in the gland, not only by diminishing the total amount of blood contained in the economy, but also possibly by a more direct depletion—for the veins of the abdomen have direct communication with those of the visceral peritoneum, and the latter in turn with those of the *serosa* of the liver, which connect with the veins of the hepatic parenchyma. This route, it must be confessed, is a very circuitous one, and this questionable location for the application is to be recommended only when bleeding is indicated by the concomitant existence of hyperæmia of the peritoneal coat, observable at times in traumatic cases. Should an appreciable tumefaction of the liver be also present in these cases in addition to great sensitiveness, then in robust individuals venesection itself may be warrantable, as this operation may bring about a rapid subsidence in the volume of the liver.

Moderately filled ice-bags, or when, on account of their weight, these cannot be borne, oft-changed cold compresses applied to the region of the liver, are also advisable in recent cases of traumatic hyperæmia, since in this affection the main indication would appear to be to produce a relaxation of the vessels, and, in accordance with the researches of Schultze,[2] there can be no

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[1] *Lersch*, Einleitung in die Mineralquellen. Bd. 1. Erlangen, 1855. S. 884.

[2] Deutsches Archiv f. klin. Med. Bd. 8, S. 504 ff.

doubt that by the aid of the above-mentioned agents, provided they are applied over a sufficient surface—both in front and behind—we may succeed in producing even in the interior of the gland a lowering of the temperature sufficient to affect the walls of the vessels.

In other forms of hyperæmia of the liver warm cataplasms (Priessnitz's compresses or cataplasms) in the vicinity of the liver serve to alleviate the subjective suffering; observations have failed to establish whether—possibly by means of the revulsive action induced by the irritation of the skin—they exercise any alleviatory influence upon the hyperæmia itself. Certain writers speak favorably of the decided results obtained in chronic cases by the application of powerful cutaneous irritants in the vicinity of the liver, while in the idiopathic form peculiar to hot climates repeated vesication has proved similarly efficacious (*vide* Treatment of Suppurative Hepatitis), as have also powerful cold douches in chronic hyperæmia[1] arising from dietetic irregularities, and in the swelling resulting from malarial fevers.[2]

The regimen of the patient should be determined in each case in accordance with known general principles, having regard to the etiological relations, the general physical condition, and the state of the digestive organs. A rapid development or augmentation of an abnormal quantity of blood within the system indicates the necessity of rest in the horizontal posture, and a restricted, bland, and chiefly vegetable diet; whereas, should the disease persist for a longer period, a strengthening, tonic treatment may often become requisite.

For the relief of the ascites resulting from the cyanotic atrophy and induration of the liver, which may become so considerable as to induce, in conjunction with the respiratory disturbances attributable to the primary disease, dangerous dyspnœa, diuretics—such as digitalis and acetate of potash—prove almost invariably insufficient or totally inoperative, while drastic cathartics are usually rendered inadmissible by the weak state of the sufferer. In such cases the *indicatio vitalis* seems

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[1] *Fleury*, Hydrothérapie. 3. éd. Paris, 1866, p. 883.

[2] *Hertz*, Vol. II. of this Cyclopædia.

only to be fulfilled by the operation of paracentesis. The prolongation of life thus obtained is, no doubt, usually but brief; yet, in a case reported as occurring in Oppolzer's clinique,[1] a patient with incompetence of the mitral and tricuspid valves, associated with atrophied nutmeg-liver, was operated upon for ascites seven times, death not supervening until six months after the date of the first puncture.

Hemorrhage of the Liver.

Fauconneau-Dufresne, L'Union médic. 1847. Nr. 88–90.—*F. Weber*, Beitr. z. pathol. Anat. der Neugebor. 3. Lief. Kiel, 1854. S. 56.—*Frerichs*, Klinik der Leberkrankh. Bd. 1, S. 395 ff.—*Bamberger*, Krankh. d. chylopoet. Syst. 2. Aufl. Erl., 1864. S. 549.—*E. Rollett*, Wien. med. Wochenschrift. Jahrg. 15. 1865. Nr. 14, 15.—*A. Steffen*, Jahrb. für Kinderheilk. N. F. 4. Jahrg. 1871. S. 333. —*L. Mayer*, Die Wunden der Leber und der Gallenblase. München, 1872. S. 63.

Hemorrhages of the liver, notwithstanding the great vascular character of this gland, are, upon the whole, of unfrequent occurrence. They may occur in consequence of solutions of continuity produced by wounds, contusion, or concussion of the organ. In new-born children they may be the result of acute obstructive hyperæmia developed during difficult labor, or in conjunction with atelectasis of the lungs. They are observed, also, at times associated with intense congestions of the liver in the malignant forms of intermittent fever peculiar to the tropics, and likewise in scurvy. It is affirmed by many authors (for example, Fauconneau-Dufresne) that obstructive hyperæmia due to other causes may also give rise to considerable hemorrhages; but this theory is not yet fully demonstrated. In exceptional cases quite a profuse loss of blood may occur from vascular, cancerous nodules situated in the liver (*vide* Rollett on Cancer of the Liver). Finally, there exist in the liver accumulations of blood whose source of origin cannot be explained by the isolated observations[2] thus far collected, though it is not im-

[1] Allgem. Wien. med. Zeitung. Jahrg. 6. (1861). Nr. 19.

[2] *Louis*, Mémoires ou Recherches anatomo-patholog. Par., 1826, p. 381.—*Andral*, Clinique médic. 4. partie. Par., 1827, p. 33.—*J. Abercrombie*, in article by *Copland*, Lond. Med. Gaz. Vol. 34, 1844, p. 507.

probable, as is surmised by Frerichs, that they may be traceable[1] to some local affection (fatty degeneration) of the vascular coats.

The symptoms of hepatic hemorrhage cannot usually be distinguished from those which are due to the hyperæmia forming the origin of the disturbance. The lesion can be diagnosticated with a certain degree of probability only when, under certain conditions that may possibly favor the supervention of hepatic hemorrhage (trauma, malignant intermittent fever, carcinoma of the liver), there results a sudden increase in the volume of the organ, attended with pain; or when a fluctuating tumor, emitting a dull percussion-note, rapidly arises almost under the eye of the observer, the symptoms of increasing anæmia appearing in a degree proportionate to the enlargement of this tumor. If the extravasation bursts through the serous coating, and escapes into the abdominal cavity, then death supervenes under symptoms of internal hemorrhage or of diffused peritonitis. The treatment consists in the local applications of cold and the administration of pain-allaying, restorative medicines.

Perihepatitis.

By this term is designated the inflammation of the peritoneal coating of the liver (*hepatoperitonitis*, *peritonitis hepatica sive velamentosa*), as well as that of the connective tissue at the hilus of the organ. The latter variety possesses clinical interest principally from the fact that it occasionally gives rise to important alterations of the *vena portæ* or the *ductus choledochus;* it will, therefore, be more properly considered under the head of Etiology of the Diseases of the Portal Vein and the Gall-ducts.

Peritonitis of the liver is, as a rule, a secondary affection. Apart from its occurrence as an accompanying symptom of general peritonitis, it is most frequently induced by diseases of the substance of the liver. It is associated constantly with diffused interstitial hepatitis, usually extending under these circumstances

[1] The hemorrhage from a large hepatic vessel (hepatic artery, twig or branch of the portal vein) that has been perforated by a corroding ulcer of the duodenum, stomach, or colon should not be included under this class, since it takes place in the adjoining organ, and not in the liver.

over the outer surface of the organ. It is developed to a limited extent at the point where abscesses, circumscribed syphilitic inflammations, or gummata come in contact with the serous envelope; it is observed less constantly over carcinoma and echinococcus seated in the periphery. Slight solutions of continuity of the serous covering from traumatic influences seldom tend to induce perihepatitis; after contusions and concussions of the liver it makes its appearance, for the most part, indeed, not directly, but only in consequence of the lesions which the parenchyma undergoes as the result of these processes. Upon the other hand, there are developed, at points where a daily recurring or persistent pressure is exercised upon the liver, regular inflammatory alterations of the serous covering, observable also upon the anterior surface in tight-lacing, and upon the blunt margin of the left lobe where there exists considerable hypertrophy of the heart. It not unfrequently happens that the inflammation extends from the right pleura and the diaphragm, from the pyloric portion of the stomach, or from an adjacent portion of the intestine, to the covering of the liver.

In case the serous coating of the liver participates in a general peritonitis, it exhibits the same anatomical changes as the remainder of the peritoneum. If this inflammation arises from local causes, it usually results — either after pre-existing fibrinous exudation, or, what is more frequently observed, without such an exudation—in a new formation of connective tissue, which gives rise at times to adhesions between the liver and the neighboring organs (diaphragm, anterior abdominal wall, colon, stomach), and, at times, to partial or diffused thickening of the serous coating itself. The substance of the liver usually undergoes no perceptible alteration in consequence of the inflammatory processes sustained by its covering; at the most, under the pressure of moderate exudations the more superficial layers become anæmic. The sharp margin may acquire a certain rotundity as a result of the retraction of the new connective tissue formed around it, and thus the figure of the entire organ may approximate to that of a globe. In rare cases the greatly thickened serous coating may form a tough capsule, which, by the action of its concentric contraction, seems to play a more impor-

tant part than the newly-formed interstitial tissue in the compression of the blood-vessels of the parenchyma.[1]

Perihepatitis makes its appearance suddenly, or comes on insidiously, according to the degree of severity of the causative agencies. In the former case it is accompanied by pain which—if the inflammation is sufficiently extensive—frequently involves the entire region of the liver, though it is more commonly restricted to a portion of this organ. This pain is brought on, or aggravated, by pressure applied from the outside, by lying upon the right side, by motions of the trunk, and, above all, by the respiratory displacement of the organ. It may in this way occasion dyspnœa, and render the physical examination of the liver much more difficult. It is to be distinguished from the pain arising from affections of the hepatic parenchyma by the fact that it is acute and lancinating, the latter being of a pressing character, and generally more dull. It should be remarked, however, that pain and great sensitiveness to pressure, quite as intense as that of acute perihepatitis, occur also in many affections of the liver that are accompanied by a very rapid increase or diminution in the volume of the gland (acute hyperæmia, acute atrophy).

Pain is often the sole symptom by means of which acute perihepatitis can be recognized. And yet fever may also not unfrequently be present, or at times a slight icterus, and in exceptional cases a peritonitic friction-sound. The latter phenomenon is, on the other hand, more frequently observable in chronic perihepatitis, especially when co-existent with some affection of the liver, as a result of which the organ has increased in volume and consistence.

Although there are no other signs of chronic hepatoperitonitis, its sequelæ may contribute to the production of very considerable disturbances. When it has given rise to extensive firm adhesions between the liver and the anterior abdominal wall, then the downward movement of the inferior margin of the gland accompanying deep inspiration ceases. If the paren-

[1] Vide *Budd*, Diseases of the Liver. Translated into German by *Henoch*, p. 133.—*Bamberger*, Krankheiten des Chylopoet. Systems. 2. Aufl., S. 495.—*Oppolzer*, Allgem. Wiener Med. Ztg. 1866, Nr. 19.—*Banks*, Dublin Quart. Jour. August, 1867, p. 231.

chyma is subjected to great pressure by the contracting capsule, then the same symptoms appear as in the second stage of cirrhosis, and the affection can scarcely be distinguished during life from the latter lesion. A similar complication of appearances is found when—as in a case observed by Frerichs (loc. cit., Bd. 2, S. 409)—the chronic inflammation has extended to the wall of the hepatic veins.

Right pleurisy may be mistaken for acute *peritonitis hepatica* when, in case of the former affection, the pain and friction-sound have their seat in front of and at the lower end of the pleural sac; still, the diagnostic aid afforded by other circumstances will usually enable us to determine whether the affection is one of the respiratory organs or of the liver.

Except in those extremely rare cases, where the perihepatitis gives rise to those serious after-effects above described, the disease is not, of itself, a dangerous one. The adhesions produced by it between the liver and the adjacent organs may even, under certain circumstances, become requisite in compensating by means of their blood-vessels for derangements of the circulation in the gland.

In acute perihepatitis—the chronic variety will not be considered from a therapeutic point of view—an alleviation of the symptoms may be frequently obtained from rest in the horizontal posture and the continued application of cataplasms or Priessnitz's compresses. In recent cases, of traumatic origin, ice-bags—when these do not prove too heavy for the patient—should be recommended rather than moist warm applications. Severe pain indicates—provided the strength be not impaired—the local abstraction of blood; in enfeebled patients, however, it calls for the subcutaneous application of morphine. Where there exists a long-continued tendency to pain, blisters frequently repeated, or painting with tincture of iodine, may occasionally afford benefit. Other remedies recommended for the relief of perihepatitis, such as calomel and the neutral salts, may be indicated by the primary hepatic disease.

Suppurative Inflammation of the Liver. Hepatic Abscess.

Hepatitis Vera sive Suppuratoria.

Bontius, De medicina Indorum. L. B. 1645, p. 3, Chap. 7.—*Fr. Hoffmann*, De inflammat. hepatis rarissima, etc. Halæ, 1721.—*W. Saunders*, Observations on Hepatitis in India. London, 1809.—*T. B. Wilson*, On Hepatitis. London, 1817.—*Campbell*, Observations on the Opinions and Practice of Dr. Saunders, etc. London, 1809.—*Griffith*, An Essay on the Common Causes and Prevention of Hepatitis in India, as well as in Europe. London, 1817.—*Abercrombie*, Pathological and Practical Researches on the Diseases of the Stomach and Intestines. London, 1823. Deutsch von G. v. d. Busch, 1833.—*Gendrin*, Histoire anatom. des inflammations. Paris, 1826. Vol. 2.—*Louis*, Mémoires ou recherches anat.-patholog. sur diverses maladies. Paris, 1826.—*Andral*, Clinique médicale. T. 4. Paris, 1827.—*Geddes*, Trans. of the Med. and Phys. Soc. of Calcutta. Vol. 6. 1833, p. 284. Schmidt's Jahrb. Bd. 6, S. 242.—*Twining*, Clinical Illustrations of the most Important Diseases of Bengal. Second Edit. Calcutta, 1835.—*Stokes*, Ueber d. Heilung d. inneren Krankh. Deutsch von Behrend. Leipzig, 1835.—*Cruveilhier*, Anat. patholog. du corps humain. Paris, 1830–42. Livre 11, 16, 40.—*Malcolmson*, Medico-Chirurg. Transactions. Vol. 21. 1838.—*Murray*, Madras Quar. Jour. July, 1839.—*Annesley*, Researches into the Causes, Nature, and Treatment of the More Prevalent Diseases of India, etc. London, 1841.— *W. Thomson*, A Pract. Treatise on the Diseases of the Liver and Biliary Passages. London, 1841.—*Murray*, London Med. Gaz. Vol. 38, p. 566.—*C. Broussais*, Recueil des mémoires de Méd., Chir. et Pharm. militaires. 1. Série. T. 55. Paris, 1843.—*Idem*, Jour. de Méd. Août et Sept., 1845.—*Catteloup*, Rec. de mém. de Méd. milit. 1. Série. T. 58. Paris, 1845; ibid. 2. Série. T. 7. Paris, 1851.—*G. Budd*, On Diseases of the Liver. London, 1845. Deutsch von Henoch. Berl., 1846. 2. ed. 1851.—*Schuh*, Zeitschr. der Gesellsch. d. Aerzte zu Wien. Febr., 1846.—*Geddes*, Clin. Illustrations of the Diseases of India. London, 1846.—*Fauconneau-Dufresne*, Revue médic. Avril, 1846.—*Parkes*, Remarks on the Dysentery and Hepatitis of India. London, 1846.—*Cambay*, Traité de la dysenterie des Pays chauds. Paris, 1847.—*Allan Webb*, Pathologia India. 2. edit. London, 1848.—*Oppolzer*, Prager Vierteljahrschrift. Bd. 13, S. 110.—*Haspel*, Maladies de l'Algérie. T. II. Paris, 1852.—*Henoch*, Klinik der Unterleibskrankh. Berl., 1852. 3. Aufl. 1863.—*Virchow*, Arch. f. pathol. Anat. Bd. 4.—*Muehlig*, Zeitschr. d. G. d. Aerzte zu Wien. Bd. 8. Nr. 6–8.—*Wunderlich*, Handb. d. Pathol. u. Ther. 3. Bd. 2. Aufl. Stuttg., 1856.—*S. L. Heymann*, Verhandl. d. physik.-medic. Ges. zu Würzburg. Bd. 5, S. 43 ff.—*Ch. Morehead*, Clin. Researches on Diseases of India. London, 1856.—*Dutroulau*, Mém. de l'Acad. imp. de Méd. T. 20.—*Rigler*, Wien. med. Wochenschr. 1856. Nr. 46 u. 47.—*Fauconneau-Dufresne*, Précis des mal. du foie et du pancréas. Paris,

1856.—*Goguel*, Des abcès du foie. Thèse. Strasbourg, 1856.—*J. Périer*, Rec. des mém. de Méd. milit. 2. Série. T. 19. Paris, 1857.—*Traube*, Deutsche Klinik. 11. Dec., 1859. Ges. Abhandl. Bd. 2, S. 940.—*Rouis*, Recherches sur les suppurations endémiques du foie. Paris, 1860.—*Lebert*, Traité d'anat. pathol. Paris, 1855–1861. T. 2, p. 253.—*Frerichs*, Klinik der Leberkrankh. Bd. 2, S. 96 ff.—*Bristowe*, Trans. of the Patholog. Soc. of London. Vol. 9.—*Tuengel*, Klin. Mittheil. v. d. med. Abth. des allgem. Krankenhauses in Hamburg aus d. J. 1862–63. Hamburg, 1864. S. 155.—*H. Cooper*, Brit. Med. Jour. May 23, 1863. Schmidt's Jahrbb. Bd. 120, S. 51.—*Bamberger*, Krankh. des chylopoetischen Systems (im Handb. der spec. Path. u. Ther., redig. v. Virchow). 2. Aufl. Erl., 1864. S. 495.—*J. R. Martin*, The Lancet, 1864. Vol. II., 8, 9.—*C. Morehead*, The Lancet, 1864. I., 20.—*Lavigerie*, De l'hépatite. Thèse. Paris, 1866.—*H. Westermann*, De hepatitide suppurat. Diss. Berol., 1867.—*Lino Ramirez*, Du traitement des abcès du foie. Paris, 1867.—*A. F. Dutroulau*, Traité des maladies des Européens dans les pays chauds. 2. éd. Paris, 1868.—*H. Rebentisch*, Beitr. z. Kenntniss der Leberkrankh. in den Tropen. Inaug.-Diss. Jena, 1868.—*Kussmaul*, Berl. klin. Wochenschr. 1868. Nr. 12.—*St. H. Ward*, The Lancet, 1868. II., pp. 141, 305, 474.—*G. Bueckling*, 36 Fälle von Leberabscess. Diss. Berlin, 1868.—*Klebs*, Handbuch der pathol. Anat. S. 426 ff.—*Traube*, Berl. klin. Wochenschr. 1869. Nr. 1. Ges. Abhandl. Bd. 2, S. 867.—*Th. Ackermann*, Virch. Arch. Bd. 45, S. 39.—*S. V. de Castro*, Des abcès du foie des pays chauds et de leur traitement chirurg. Paris, 1870.—*Heinemann*, Virch. Arch. Bd. 58, S. 180.—*Gallard*, L'Union médic. 1871. Nr. 94 sqq.—*Gysb. Luchtmans*, Mededeelingen over het samentreffen van leverettering en dysenterie. Akad. proofschrift. Utrecht, 1872.—*van Riemsdyk*, Leverettering in de tropische gewesten. Akad. proofschrift. Utrecht, 1873.—*M. Heitler*, Wien. medic. Presse, 1873. Nr. 24–26.—*McConnell*, The Indian Annals of Med. Sc. July, 1873. Jahresber. von Virchow und Hirsch f. 1873. II. S. 167.—*A. Thierfelder*, Atlas der patholog. Histologie. 3. Lief. Taf. XV. Fig. 1–3.—*Curschmann*, Deutsche Klinik, 1874. Nr. 48, 50, 51.—*Berenger-Feraud*, Giorn. Veneto di Sc. med. 1875. Nr. 1. Allgem. medic. Centralzeit. 1875. St. 21.

Historical Account.

The ancient pathologists assigned a very comprehensive definition to hepatitis, including under that head almost all affections of the liver, especially such as are attended by pain. At the sick-bed, therefore, the diagnosis of hepatic inflammation was much too frequently made, affections of the adjacent organs —those of the right pleura, the right kidney, the stomach, etc.— being often confounded with it.

In even the works of the old Greek physicians cases of genu-

ine hepatitis are described, being treated especially from a semeiological point of view. Hippocrates (Aphor. VII., 44) gives an account of the opening of an hepatic abscess by means of the actual cautery, while in Celsus may be found the statement that many were in the habit of laying them open by means of the knife. The way was first paved for a more accurate knowledge of the disease by the pathologico-anatomical researches made in the sixteenth and seventeenth centuries. In the list of cases given by Bonet (Sepulchretum, Lib. III., Sect. 17), and Morgagni (Epist. 36), under the title *De Hypochondriorum Tumore et Dolore*, are represented—almost exclusively by examples—the different directions by which an hepatic abscess may make its way to the surface. For the most numerous observations on suppurative hepatitis we are indebted to those physicians who have had an opportunity of practising in warm regions, where these affections are of much more frequent occurrence than in the temperate zone.

Etiology.

The consideration of suppurative hepatitis of warm climates will be omitted at this point, in order that the question of the origin of the affection may be hereafter made the subject of special discussion.

In the temperate zone the disease forms one of the rare affections. According to Bueckling, during a period of five years, hepatic abscesses were met with in the Berlin Pathological Institute in 36 out of 2,463 autopsies—that is, in 1.5 per cent. As causes of the disorder, the following influences are recognized:

1. *Mechanical Injuries.*—Traumatic hepatitis is developed either from penetrating wounds of the liver, complicated usually by the presence of a foreign body; or from ruptures, such as result from a contusion of the organ induced by a blow, kick, or fall upon the region of the liver; and by a severe concussion caused by a fall from a great height, where, however, the individual falling does not strike the vicinity of the liver. The strong pressure, moreover, to which the liver is subjected in certain attitudes of the body, if long maintained, may apparently

induce this disease. Borius[1] observed an acute hepatitis (terminating in abscess) occurring in a woman, thirty-eight years of age, previously quite healthy, that was developed immediately after she had walked a German mile in cold, rainy weather, carrying a child of three years upon her left hip, and an open umbrella in her right hand.

It is, however, upon the whole, comparatively seldom that mechanical injuries give rise to this disease; out of seventeen cases observed by Louis and Andral (ll. cc.), in one instance only could this cause be demonstrated. In the literature of the last thirty years to which I have been able to obtain access, I have found, in addition to the case of Borius just quoted, eleven others of traumatic origin.[2] Even serious lesions of the liver may frequently be unattended by any inflammation. Frerichs treated a railway laborer, whose right hypochondrium had been crushed between the buffers of two railway-wagons, and who in consequence of this became jaundiced, without observing the development of any hepatitis. In the Reservelazareth of Rostock (1870), in the case of a soldier with a bullet-wound penetrating transversely both hypochondria, bile was discharged for a long while from the opening upon the right side; complete recovery ensued without the supervention of any inflammatory symptoms in the liver.

2. *Extension of Inflammatory and Ulcerative Processes from Contiguous Structures.*—The view put forth by Broussais,[3] which Andral also shared (loc. cit., p. 263), that a gastro-enteritis, which had extended from the duodenum into the biliary ducts, could spread still further into the substance of the liver, thus setting

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[1] Gaz. des Hôp. 1866. Nr. 49.

[2] *Weitenweber*, Oesterreich. Wochenschrift, 1844. Nr. 14.—*Renaud*, L'Union méd. 1850. Nr. 37 (bei *Bouchut*, Kinderkrankh., übers. v. Bischoff. Würzb., 1854. S. 647).—*M. Simon*, Bull. de Thérap. LVII. 298, 345. Oct., 1859.—*Traube*, Deutsche Klinik, 1870. 7. Apr. Gesammelte Abhandl. II. S. 963.—*Wolfes*, Deutsche Klinik, 1864. 1.—*Greenhow*, Brit. Med. Jour. Sept., 1864.—*Loewer* (aus *Traube's* Klinik), Berl. klin, Wochenschr. 1864. Nr. 48.—*Huet*, Nederl. Tydschr. voor Geneesk. 1867. I., p. 648.—*Fischer*, Zeitschr. f. Wundärzte u. Geburtsh. 1868. Heft 2.—*Volz*, Würtemb. medic. Correspondenzbl. 1870. Nr. 4.—*Curschmann*, loc. cit.

[3] His proposition (149) declares that hepatitis follows gastro-enteritis when the latter is not caused by external violence.

up a hepatitis, and, in fact, be its most frequent cause, is now generally abandoned. On the other hand, there have been observed cases of typhoid fever followed by hepatic abscesses proceeding from ulcerations in the walls of the twigs of the *ductus hepaticus* (Klebs, loc. cit., S. 480). Cases are rather more frequent in which ulceration of the intra-hepatic bile-ducts, caused by calculi or wandering round worms, extends into the contiguous parenchyma of the gland.

Cases of this sort, caused by gall-stones, are described by Goguel (loc. cit., p. 7), Lebert (Traité d'Anatomie pathol., T. 2, p. 320, and Deutsches Arch. f. klin. Med. Bd. 6, S. 518), Frerichs (loc. cit., S. 431. Beob. 67), Cohnheim (Berl. klin. Wochenschr. 1867, S. 539). Six cases in which the presence of round worms had led to the formation of abscesses are to be found in Davaine, Traité des Entozoaires, p. 165–171. Among these is the case reported by Kirkland (Case 36), in which an abscess, pointing at the level of the twelfth rib, on the right side, discharged a round worm, together with considerable pus.

But simple distention of the bile-ducts, in consequence of closure of the *ductus choledochus*, when long continued, also gives rise to the formation of hepatic abscesses, induced probably by consecutive inflammatory processes in the walls of the distended finer bile-ducts, and possibly by their rupture.[1] Finally, are to be mentioned the very rare cases in which deposits of pus form around dilated gall-ducts, which communicate with the cavity of an echinococcus cyst, and have been filled by its contents.[2]

By the penetration of a perforating ulcer of the stomach into the left lobe of the liver, the loss of substance at this point gives rise to the formation of an excavation, which usually opens toward the stomach; and that this can change, in exceptional cases, into an independent, closed, and active abscess, by the cicatrization of the gastric ulcer, seems to be demonstrated by an observation made at Lebert's clinique, and reported by Wyss.[3]

3. *Emboli in the Blood-vessels of the Liver.*

a. *In the Portal Vein.*—After injecting mercury into the

[1] *Pentray*, Considérations sur certains abcès du foie consécutifs à l'angiocholite intra-hépatique. Thèse de Paris; and *Magnin*, De quelques accidents de la lithiase biliaire, etc. Thèse de Paris. Virchow-Hirsch Jahresber. für 1869, S. 153.

[2] *Bueckling* (loc cit. S. 20) describes the result of the autopsy in two such cases.

[3] Wiener medic. Presse. 1865. Nr. 50–51.

mesentèric vein, Cruveilhier[1] found collections of pus in the liver, each of which contained a globule of the metal. Cohn[2] reports that he has often produced abscesses in the liver by the injection of pus into the portal system. Hepatic abscesses are likewise formed when, from thrombi occurring in any part of the portal system, fragments, broken off by puriform or putrefactive changes, are carried into its finer ramifications. Suppurative and ulcerative conditions in the regions about the roots of the portal vein furnish the most common starting-points of this process. In some of the cases included under this category these vessels are filled, for a greater or lesser distance, with clots and the products of their decomposition (the so-called suppurative pyle-phlebitis), so that the mechanism of the origin of the liver disease is easily seen. In other cases, on the contrary, the process set up by the embolus seems to leave no trace behind. There are, at least, many observations to be found in the literature of the subject, in which the development of abscesses in the liver is, from the condition of the case, in all probability traceable to the formation of pus in some parts of the roots of the portal vein, although a broken-up thrombus is nowhere to be found in the portal system. We must hence conclude that, at the time of the examination, the remains of the thrombus in the primary as well as of the embolus in the secondary pathological deposit were already completely destroyed.

Each of the organs from which blood flows into the portal vein may become the starting-point for the production of embolic hepatic abscesses.

In new-born children it sometimes occurs in consequence of phlebitis umbilicalis. Mildner[3] relates a case of this sort in which the pus extended into the portal ramifications of the liver, and the whole left lobe was converted into an abscess. H. Meckel[4] speaks of numerous small abscesses in the liver, caused by inflammation of the umbilical vein, when the pus makes its way into the afferent veins of the right

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[1] Anat. pathol. Liv. XI.

[2] Klinik der embol. Gefässkrankh. S. 506.

[3] Prager Vierteljahrschrift. 1848. Bd. II. S. 88.

[4] Annalen d. Char. IV. S. 244. Compare also *Buhl* in *Hecker* u. *Buhl*, Klinik der Geburtsk. Leipzig, 1861. S. 274.

lobe. Busk (in Budd, loc. cit., p. 67) saw numerous walnut-sized hepatic abscesses along with a large infarction of the spleen; the *vena lienalis* contained in its roots and trunk a puriform fluid and scattered lymphatic deposits. In a case of encysted pyothorax, reported as occurring in the Leipzig Pathological Institute, there was found a purulent infiltration of the diaphragm at the base of the left lung, and an abscess in the adherent spleen; pus in the splenic vein, and abscesses in the liver, varying in size from that of a pea to a hazel-nut. In one of the cases of hepatic abscess, collected by Bueckling (loc. cit., S. 23) from the protocols of the Berlin Pathological Institute, the *vena pancreatica*, which could be followed into a pus cavity of the *pancreas* the size of a cherry, was colored green at the part where it emptied into the portal vein, and filled with partly fresh and partly old thrombi which extended into the portal vein. In the case of *phlegmonous gastritis* with embolic deposits in the liver (and in the lungs), which Ackermann (loc. cit.) has described, not only were the numerous veins of the walls of the stomach and the trunk of the *vena gastro-epiploica dextra*, but also the two main branches of the portal vein and its longer ramifications, filled with thrombi, which were in great part puriform. Ulcerations of the *mucosa of the digestive tract* lead but very seldom, relatively to the great frequency of their occurrence, to the formation of abscesses in the liver. Observations in cases where such ulcerations were coexistent with carcinomatous or simple *gastric ulcer*, though not directly connected therewith, have been made by Louis (loc. cit., Obs. 4), Andral (loc. cit., Obs. 27–30), Murchison,[1] and Finlayson;[2] the connection of the two diseases by means of the portal vessels has, however, not been demonstrated in these cases. In one of Bamberger's[3] cases, besides a fresh gastric ulcer and innumerable abscesses of the liver, the portal vein was found to be filled with a broken-down coagulum of mixed shades; but there was also in the spleen a large deposit of sanious pus; so that it appeared doubtful whether the latter or the gastric ulcer had caused the thrombosis of the portal vein. Sometimes the *ulcus ventriculi* causes the formation of hepatic abscesses in a roundabout way, as when, in consequence of its perforation, an encysted purulent deposit takes place in the peritoneum. Such cases have been reported by Seymour[4] and Leyden.[5] So far as we know, no observations have ever been made tending to show that *tubercular ulcerations of the intestines* may lead to the development of hepatic abscesses. Bristowe (loc. cit.) reports that, of 167 cases of tubercular ulceration of the intestines, 12 showed small tubercular cavities in the liver. The latest monographs upon abdominal typhus[6] mention hepatic abscesses as an infrequent sequel, without, however, giving examples. According

[1] Transactions of the Pathological Society. XVII. 154.

[2] Glasgow Med. Journal. Feb., 1873. Jahresber. v. Virchow u. Hirsch. 1873. II. 167.

[3] Krankheiten des chylopoet. Systems. 2. Aufl. S. 258.

[4] Med. Gaz. Nov. 24, 1843.

[5] Berl. klin. Wochenschr. 1866. Nr. 13.

[6] *Griesinger*, Infectionskrankheiten. 2. Aufl. S. 202. *Liebermeister*, This Cyclopædia. Vol. II. Part 1st, p. 166.

to a note of Leudet,[1] such cases have been noticed by Louis, Andral, Barth, Tardieu, and others. Bueckling (loc. cit., pp. 21 and 22) refers to two cases in which the formation of hepatic abscesses seems to have been caused by typhoid intestinal ulcerations. In an observation mentioned by Tuengel (loc. cit., Nr. 6), a sanious deposit was formed by the suppuration of a lymphatic gland near the cæcum, which had perforated a root of the *vena mesenterica superior*, while the typhoid ulcerations of the intestines were all healed at the time of death, which took place two months after the beginning of the sickness. Hepatic abscesses may be sometimes caused by the chronic suppuration of the submucosa or mesentery, following *dysentery*. They occur only exceptionally in conjunction with *catarrhal* and *follicular ulceration* of the lower portions of the intestines.[2] They are observed with greater relative frequency in ulcerations of the *cæcum* and *appendix vermiformis*, especially when perforation of the latter has led to the formation of an encysted deposit of sanious pus. In such cases, which have been described by Buhl,[3] Tuengel (loc. cit., Nr. 1, 3, 5), Traube (ll. c.c.), Westermann,[4] Malmsten and Key,[5] G. Riedel,[6] and others, the thrombus in the mesenteric veins in the cæcal region extended along the portal vein into its ramifications in the liver. In the case observed by Payne,[7] where the processus vermiformis was firmly attached to the peritoneum of the iliac fossa and the cæcum, and ulcerated at its blind end, the trunk of the *vena mesenterica superior* formed the seat of the only coagulum, which was prolonged into the portal vein. In another case of the same writer, a concretion was found in the processus vermiformis surrounding a pin whose head extended into the cæcum; the processus vermiformis, bent around and adherent to the cæcum, showed some thickening of the walls, but was otherwise free from inflammatory changes; it could not be demonstrated that the blood-vessels were at all implicated.—Wounds of the *rectum* are sometimes followed very suddenly by a metastatic hepatitis. Dance[8] found hepatic abscesses in two cases in which an operation (cauterization of a carcinoma, division of a fistula) had been performed but a short time before; Pirogoff,[9] likewise, in two cases after operation for *prolapsus ani*. Cruveilhier (loc. cit.) saw a number of fresh hepatic abscesses in a man who died five days after the forcible replacement of a neglected

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[1] Clinique médicale. Par., 1874, p. 84.

[2] Similar cases reported by *A. Faller* (Lond. Gaz. Apr., 1847) and *Everett* (ibid., May, 1847).

[3] Zeitschrift für ration. Med. 1854. S. 348.

[4] *H. Westermann*, De Hepatit. suppur. Diss. Berol., 1867. *Bueckling's* sixth case (loc. cit. S. 21) is probably the same.

[5] Nord. med. Arkiv. I. 2, S. 20. Schmidt's Jahrbb. Bd. 149, S. 171.

[6] Ein Fall v. Pyophlebitis in Folge v. Perfor. d. Proc. vermif. Berlin, 1873. A case of pyophlebitis following perforation of the vermiform appendix. Berlin, 1873.

[7] Trans. of the Pathological Soc. Vol. XXI. p. 231.

[8] Arch. génér. T. XIX. p. 172.

[9] Grund. d. Allgem. Kriegschirurgie. Leipzig, 1864. S. 957.

prolapsed rectum. *Localized purulent peritonitis* induced by causes other than those above mentioned sometimes also gives rise to abscesses in the liver, as in the two cases reported by Dance[1] of suppuration in a portion of the omentum which could not be replaced in herniotomy. Winckel[2] saw innumerable hepatic abscesses, and the ramifications of the portal vein filled with clots and a puriform mass, in a puerperal patient in whom a circumscribed sanious exudation consecutive upon a diffused peritonitis had been retained between the uterus and bladder. If, as Bamberger teaches, hepatic abscesses may be caused by suppurative processes in the *uterus* and *ovaries*, through embolus of the portal vein, then the material can also be furnished by softened thrombi of the *plexus uterinus*, which is in communication with the other pelvic plexuses, and through them with the *vena hæmorrhoidalis superior*.

The thrombotic process rarely attacks directly the *trunk of the portal vein.*

In the case described by Busk (in Budd, loc. cit., p. 161), where both lobes of the liver were studded with numerous abscesses, there was found a considerable deposit of pus in the transverse fissure, while suppurating lymph-glands lay in direct contact with the trunk of the portal vein, which was partly ulcerated and filled with pus. In a case of offensive cancroid of the œsophagus, which had burrowed behind the stomach and perforated the trunk of the portal vein, Tuengel[3] observed a dirty yellowish gray fibrinous clot in the latter vessel lying in contact with the wall, while the liver contained purulent deposits.

Finally, the emboli may originate from thrombi formed in the *ramifications of the portal vein* by the influence of other hepatic disorders.

Louis (loc. cit., Obs. 5), Bright,[4] and Budd (loc. cit., p. 65) long since observed in ulcerations of the gall-bladder or *ductus choledochus*, the existence of hepatic abscesses which did not communicate with the biliary passages. Leudet (loc. cit., p. 7) cites a case from Lebert in which the liver was riddled with abscesses, the gall-duct distended with concretions, and the twigs of the portal vein filled with thrombi for the most part in a puriform state. In a case observed by Leudet himself (ibid.), at a point in the left branch of the portal vein, where it was compressed by the left gall-duct which was distended by a calculus, there lay a plug softened in the centre; the finest twigs of the portal vein contained purulent fluid, and the adjacent parenchyma of the liver showed, in places varying in

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[1] *Loc supra citat.*

[2] Die Pathol. u. Ther. des Wochenbettes. 2. Aufl. Berlin, 1869. S. 252.

[3] Virchow's Archiv. Bd. 16, S. 359.

[4] Guy's Hospital Reports. Vol. I., p. 630.

size from a pea to a hazel-nut, the beginning of the suppurative process. In another of Leudet's cases (ibid., p. 15), where an echinococcus cyst communicated with a large branch of the portal vein, the latter contained clots, and numerous small purulent deposits were found in the liver.

Notwithstanding the coexistence of suppuration in the domain of the portal vein with hepatic abscesses, there may be conditions rendering it doubtful as to whether the latter proceed from the former by the process of embolism. In a case described by Kussmaul (loc. cit.) of a cachectic female, fifty-four years old, numerous abscesses, from the size of a pea to that of a nut, were found in the right lobe of the liver, which originated in the adventitia of the portal twigs; also deposits of pus between the folds of the mesentery, and a very great number of submucous abscesses. After careful consideration of the possibilities which might serve to explain the genetic connection of the suppuration in the three different localities, Kussmaul and R. Maier[1] were led to consider these collective suppurations as effects of a single cause, namely, the cachexia; since, according to the clinical observations, the intestinal disease could not be shown to be the primary affection.

b. *Embolus in the Arteria Hepatica.*—Cohn[2] observed numerous small abscesses in the periphery of the liver after the injection of unfiltered pus into the thoracic aorta. Doubtless those hepatic abscesses, which appear (extremely seldom, it must be admitted) in the train of ulcerative endocarditis and of gangrenous processes in the lungs, originate in this manner.

In a case, described by Virchow,[3] of gangrenous infarction of the lungs, associated with hæmoptysis, putrid clots were formed in the pulmonary veins, by detached fragments of which the *arteria mesenterica superior* was plugged, and metastatic gangrenous deposits were produced in the heart, brain, liver, spleen, kidneys, and skin. R. Meyer[4] has reported from Biermer's *clinique* a case of putrid bronchitis, in which he found three abscesses in the left anterior lobe of the cerebrum, and the same number in the right lobe of the liver. In a case observed by the same author,[5] at Griesinger's clinique, of *endocarditis ulcerosa*, the liver, spleen, and kidneys, con-

[1] Arch. der Heilkunde. Bd. 8, S. 25.

[2] Klinik der embol. Gefässkrankheiten. S. 489.

[3] Virchow's Archiv. Bd. 1, S. 332. Gesamm. Abhandlungen. S. 420.

[4] Berl. klin. Wochenschrift. 1868. Nr. 42, 43.

[5] *R. Meyer*, Ueber Endocarditis ulcerosa. Zürich, 1870. S. 30.

tained quite a number of infarctions. Bueckling (loc. cit., S. 22) gives the result of the autopsy of a case of endocarditis in which the liver, besides many other organs (heart, thyroid gland, the cortex of the brain, and the spleen), displayed metastatic deposits. Ross and Osler [1] saw a very great number of hepatic abscesses caused by emboli from an aneurism at the bifurcation of the *arteria hepatica*.

The presence of an embolus in the *arteria hepatica* has been frequently assumed in those cases where, after suppuration, hepatic abscesses have supervened in some other portion of the body, the veins of which do not communicate with the portal vein. But there are very weighty objections to such an assumption. In order to pass from the venous system into the hepatic artery, the emboli must traverse the pulmonary circulation. Where in addition to the metastases in the liver, others are likewise found in the lungs, it is indeed possible that fragments detached by the blood-current from the secondary thrombi of the pulmonary veins, and not the primary embolus, are washed along into the hepatic artery. It must be admitted, however, that no one has, as yet, reported any observations from which it may be with certainty concluded that this process has taken place.[2] Still, the circumstance that not unfrequently the deposits in the liver are, according to their anatomical arrangement, clearly more recent than those in the lungs, points to this theory. But the most difficult question is, whether in such cases, where the lungs remain free from metastases, the emboli originating in the peripheral veins are transported into the liver. If the little fragments of thrombi or pus-flocculi traverse the pulmonary circulation, their diameter must be less than the calibre of the pulmonary capillaries; the attempt has, therefore, been made to explain their retention in the capillaries of the liver, by assuming a subsequent enlargement from the deposit upon them *while in transitu* of fibrine from the blood.[3] This hypothesis likewise,

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[1] Canada Med. and Surg. Journal. July, 1877.

[2] *C. Heine* (Langenbeck's Archiv., Bd. 7, S. 421) indeed says that he has generally succeeded in obtaining evidence of the origin of the metastatic deposits in the brain, liver, spleen, etc., from the wedge-shaped infarction of the lungs; yet, he fails to cite a single case affording proof of his assertion.

[3] *Stich*, Annalen d. Charité-Krankenhauses. Bd. 3, S. 236.—*O. Weber*, Deutsche Klinik. 1864. S. 463.

although perhaps in itself admissible, has not as yet been proved. The theory of O. Weber,[1] supported by experiments, that in the direct merging of the terminal ramifications of the arteries in the rootlets of the veins, such as has been observed in the lungs by this investigator, a way is furnished by which even quite large emboli can pass from the systemic veins into the hepatic artery, appears to rest upon better foundation.

Those hepatic abscesses which have usually been thought to be produced in the manner above indicated, from suppuration in the periphery of the systemic venous system, are decidedly of the most common occurrence in the temperate zone. They form one of the concomitants of so-called pyæmia, and appear in all the manifold diseases in which this lesion is consecutively developed. They are, however, far less frequent than the pyæmic metastases of the lungs. Waldeyer[2] found hepatic abscesses in only six per cent. of those who died of surgical diseases, while embolic deposits in the lungs were present in more than two-thirds. According to the obervations of Klebs,[3] thirty-two cases with metastases in the lungs occurred to eight in the liver.[4]

Generally, when hepatic abscesses are found along with *suppuration of bone*, this is to be explained, as Cruveilhier[5] and Stromeyer[6] have already shown, by the fact that the veins of the bones, on account of their firm attachment to the rigid tissue, do not collapse, and hence are more apt than the veins of the soft parts to favor the formation of thrombi, and through these the existence of metastases. This will serve to explain in part the assumed connection between the head and liver insisted upon by the older surgeons, such as Desault and Bichat. There exists, however, no foundation for this opinion, for it has been shown

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[1] Deutsche Klinik. 1864. S. 464 u. 465: Experiment 1 und 7 a. *Pitha* und *Billroth*, Handb. d. allg. u. spec. Chirurgie. Bd. 1. Abth. 1, S. 87.

[2] Virchow's Archiv. Bd. 40, S. 380, 408.

[3] Beiträge zur pathol. Anatomie der Schusswunden. Leipzig, 1872. S. 118.

[4] The observations of *Pirogoff* (Grundz. d. allgem. Kriegschirurgie, Bd. 1864, S. 957), who, in seventy autopsies of pyæmic cases, found hepatic abscesses in more than fifty, differ very widely from the usual experience.

[5] Anat. pathol. Livr. XI.

[6] Handb. d. Chirurgie. S. 7.

that hepatic abscesses do not occur any oftener in *wounds of the skull* than in general osteomyelitis; and the hairy scalp is one of the localities in which suppurating wounds most frequently give rise to pyæmia.

Still, hepatic abscesses in cases of pyæmia are not always to be considered as metastases from the original suppurative deposit. Virchow[1] has shown by several instructive instances that they are sometimes produced by embolism of the portal vein, the origin of which is to be found in thrombi formed independently of the disease tending to pyæmia in the dilated veins of the pelvis (plexus vesicalis) or of the mesentery, but which have first undergone a puriform fusion through the influence of the pyæmic condition of the blood (ichorrhæmia). In all probability the formation of hepatic abscesses might be very frequently explained in this manner, if the venous plexus of the pelvis were carefully examined in every case of pyæmia with a view to determining the presence of marantic or dilating thrombi.

c. *Embolus by Way of the Hepatic Vein.*—The fact that twigs of the hepatic artery in the immediate vicinity of hepatic abscesses very seldom contain thrombi, which, on the other hand, are found quite frequently in those of the hepatic vein, has raised the question whether or not, under certain conditions, the infecting masses may make their way from the inferior vena cava through the hepatic vein, and thus give rise to abscesses in the parenchyma of the gland. H. Meckel[2] has shown that the occurrence of mechanical metastasis through the hepatic vein is not very infrequent. According to the experiments of Magendie, Gaspard,[3] Cohn,[4] and Frerichs (loc. cit., S. 108), quicksilver injected into the jugular vein can flow into the hepatic veins, and, as Gaspard and Cohn have found, may even produce abscesses in the liver. Cohn is quite right in his objection to the conclusive force of this experiment, because the little globules of quicksilver are too heavy and too mobile to be compared to the ordi-

[1] Gesammelte Abhandlungen. S. 570, 572, 623. A case probably analogous is reported by *Bueckling* (loc. cit., S. 14. Nr. 19).

[2] Annalen des Charité-Krankenhauses. Bd. 4, S. 234.

[3] Journ. d. Physiol. experiment. I. pp. 168, 243.

[4] Klinik der embol. Gefässkrankheiten. S. 484.

nary emboli of diseased bodies. Heller[1] has sought to answer this objection by the insertion into the jugularis of a rabbit, without resorting to any greater force than that employed by Cohn in his experiment, of fine wheat meal which he had covered with Canada balsam in order to prevent its swelling, and then compressing the thorax rhythmically for a few times, succeeded in finding a few particles of the meal in the veins of the diaphragm, as well as in the finer twigs of the hepatic vein. According to the view of this author, a reflux takes place in the hepatic veins under the same conditions as it does in the jugular vein; that is to say, when the intra-thoracic exceeds the atmospheric pressure upon the vein, as is the case, for example, in coughing, as well as generally in each expiration, which is induced mainly by muscular action and not by the elasticity of the lungs. Now, the contraction of the abdominal muscles, by which the complex process of expiration is mainly effected, exerts at least as great a pressure upon the contents of the abdominal cavity as upon that of the thoracic. The compression of the thorax employed by Heller in his experiment was, therefore, very well designed to drive back the venous blood from the thorax to the abdominal cavity, there being no contraction of the abdominal muscles, but for this very reason it could not be compared to the action of active expiration.

A second weighty objection which Cohn brought against the theory of refluent embolus, viz., that no one had demonstrated for a certainty the presence of floating bodies in the hepatic vein, is, on the other hand, fully met by an observation adduced by Heller. This relates to a case of ulcerative carcinoma of the intestine with secondary carcinoma of the mesenteric, retro-peritoneal and mediastinal lymph-glands, and with diffuse suppurative peritonitis in a case of emphysema; it was here found that, while the liver was otherwise free from cancerous metastases, a minute hepatic vein contained an unquestionable cancerous thrombus loosely attached to the vascular wall; in its immediate neighborhood the parenchyma was strongly hyperæmic, and contained hepatic cells presenting within perfectly clear struc-

[1] Deutsches Archiv f. klin. Med. Bd. 7, S. 127.

tures mostly circular. Heller considered this thrombus to be an embolus, and thought it most probable that it originated in the mediastinal lymph-glands. If this conclusion is accepted, his observation possesses an especial interest with reference to the above question, in that it affords us a glimpse of the conditions under which an embolus can most readily occur in the hepatic vein. In Heller's case, in addition to the carcinomatous affection, we see two other diseases, viz., emphysema and acute peritonitis, both of which notably impair the freedom of the respiratory movements of the diaphragm, and weaken to a corresponding extent an essential factor in the hepatic circulation. In the latter lesion especially it is well known that the breathing is extremely superficial, and, moreover, the speed of the blood-current in the numerous roots of the portal vein is reduced by the exudation, the meteorism, and the inflammatory œdema of the serosa; as is that of the general circulation by the impairment of the propulsive action of the heart. Under such conditions it is quite possible that the blood may flow so sluggishly through the hepatic vein that a body of greater specific gravity than the blood-corpuscle, as, for example, a cancerous particle, may move in a direction opposed to that of the blood-current until it is stopped by the narrowness of the vessel in which it floats. And in the case in question the condition of the parenchyma of the liver in the immediate vicinity of the vein containing the thrombus fully justifies the assumption that the embolus did not reach the place where it is found until the last days of life; that is to say, not until after the appearance of the peritonitis.

While readily acknowledging, therefore, the service of Heller in demonstrating the existence of the refluent embolus, still we cannot yet accept his conclusion, that in hepatic suppuration not attributable to primary disease either in the domain of the portal vein, or the lungs, or the left cavities of the heart, the cases characterized by numerous extensive deposits are to be attributed to such emboli. Where the above-mentioned conditions of the circulation requisite for the production of refluent emboli—among which the insufficiency of the heart manifestly takes the first place—are co-existent with structures in the blood of the

vena cava suitable for the production of emboli, life would only in very exceptional cases be prolonged for a sufficient length of time to permit the formation of large hepatic abscesses. The following case, which occurred in the Leipzig Pathological Institute, supports this view: A person of hemorrhagic tendencies, about fifteen years old, upon whom the subclavian vein and artery had been tied on account of exhausting hemorrhage from a wound in the hand, experienced during the last days of his life repeated chills; at the post-mortem examination there were found, together with putrid thrombosis of the subclavian vein, numerous miliary abscesses in the liver, which could be seen even macroscopically to be located in the centre of the acini.[1]

4. Whether pyæmic suppurative deposits in the liver can often occur in consequence of *changed condition of the blood* (pyæmic krasis, ichorrhæmia), is a question that cannot be answered any better now than when first raised by Virchow.[2] Answered in the affirmative more frequently by surgeons than by pathological anatomists, it has taken a somewhat different shape in consequence of the labors of Klebs and his successors.

Klebs[3] has arrived at the conclusion, based upon observations in numerous autopsies of individuals dying of pyæmia and septicæmia supervening upon gunshot wounds, that the origin of metastatic hepatic abscesses depends upon the presence and multiplication of parasitic organisms, which he describes under the name of micrococcus septicus (and which F. Cohn has classed

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[1] A further argument for the possibility of the refluent embolus has been brought forward very recently by *L. Diemer* (Ueber die Pulsation der V. cava inf. in ihrer Beziehung zu pathologischen Zuständen der Leber. Inaug. Diss. Bonn, 1876). This author has demonstrated by experiments upon living rabbits that in the systole of the right auricle a small portion of its contents is regularly poured into the inferior cava. Hence it follows that whenever the evacuation of the auricle into the right ventricle is obstructed (by cardiac or pulmonary disease), the pulsation of the inferior cava must be increased in force, and propagated as far as the capillary rootlets of those trunks of the hepatic venous system which join the cava at an acute angle. Under such conditions, according to *Diemer's* opinion, foreign bodies floating in the blood of the right auricle may be turned into the inferior cava by the regurgitating blood-current, and make their way into the hepatic vein.

[2] Gesammelte Abhandlungen. S. 703, 705.

[3] Beiträge zur patholog. Anat. der. Schusswunden. Leipzig, 1872. S. 113 ff.

as micrococcus septicus among the globular bacteria[1]). These are thought to penetrate the blood-vessels and lymphatics from the surface of the wound, and to be conveyed by the blood-current into the internal organs. According to Klebs's theory, metastatic abscesses in the liver are formed by a great development of algoid spores in the capillaries at the point affected, which fill up and distend the vessels, cause destruction of the cells and parenchyma of the liver, and finally lead to the formation of pus, the development of the fungus ceasing when the suppuration commences. Birch-Hirschfeld[2] has partially confirmed the results upon which Klebs's theory is founded, in that, according to his observations, the bacteria are already present in the capillaries of the liver before the beginning of the suppurative process; and has demonstrated, moreover, during the lifetime of the diseased individual, the presence of this fungus in the secretion of the wounds as well as in the blood, partly free and partly on and in the white corpuscles; and finally, by his experiments with the subcutaneous injection of pus upon rabbits, reaches the conclusion that metastatic suppuration only occurs when the pus employed contains globular bacteria.

If, therefore, it is considered probable, although indeed not proven, that the bacteria stand in a causal relation to pyæmic hepatitis, there still remains, as it seems to me, a very important problem unsolved. The mere demonstration of micrococci in the blood is quite as inadequate to explain the origin of circumscribed pus deposits as is the theory of a chemical alteration of the blood. How does it happen that the micrococci, which go with the blood to all parts of the liver, find only in special parts of the organ the requisite conditions for their increase to such an extent as to cause by their presence the production of pus? This result is not to be accounted for by assuming the action of a special local cause at these points. Nothing indicates that any chemical action can constitute this cause, and it is much more probable that the fungus is detained by a mechanical process. Possibly an influence may here be exerted by the white blood-

[1] Bacterium punctum of French authors.—TRANSL.

[2] Archiv der Heilkunde. Bd. 14, S. 214, 234.

corpuscles loaded with bacteria, which Birch-Hirschfeld[1] found so considerably increased in volume that he thought them destined to play an important part in the origination of embolic metastases. Such metastases can occur in the liver the more readily since the cloudy swelling of the liver-cells, which is invariably present in pyæmia, induces narrowing of the capillaries, which may here and there very easily reach such a degree as to render the calibre of the vessel insufficient for the passage of such enlarged blood-corpuscles.

According to the evidence of trustworthy observers (Frerichs, Bamberger, Cloetta,[2] Duhamel,[3] Heaton,[4] and others), there occur in temperate climates cases of suppurative hepatitis in which, notwithstanding the most careful investigation and review of the conditions observed during sickness and after death, it is impossible to determine with certainty the existence of any of the etiological factors above alluded to. Despite all this, it is still questionable whether in such cases the disease is to be considered as primary: for, however carefully we may inquire into the previous history, the patient not unfrequently forgets or conceals some circumstance, in his opinion insignificant, but which, in an etiological respect, is of the greatest importance. The patient of Curschmann, suffering from the overpowering effects of the wound on the head received in an affray and that bled profusely, had lost all recollection of a kick in the epigastrium simultaneously inflicted, and yet the affection of the liver could be diagnosticated only from the latter circumstance, not from the wound upon the head. Furthermore, we can hardly exclude with complete certainty the possibility that a thrombosis of the portal vein may have been the cause. Thus, for example, a small patch of peritonitic inflammation, together with the phlebothrombosis to which it has given rise, may be healed long before the disappearance of the consecutive hepatitis, and its cicatrix be easily overlooked at the post-mortem examination. Finally, it may not unreasonably be assumed that an enlarged echino-

[1] Archiv der Heilkunde. Bd. 13, S. 401.

[2] Schweizerische Zeitschrift für Heilkunde. Bd. 2, S. 162.

[3] Gaz. des Hôp. 1866. No. 15.

[4] Brit. Med. Jour. July 3, 1869.

coccus cyst is occasionally mistaken for a spontaneous hepatic abscess.[1]

If we turn now to the suppurative hepatitis of warm climates the following facts relating to the geographical distribution of the affection, have been collected by Hirsch[2] from investigations

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[1] In the paper of *C. Baerensprung* (Hepatic Abscess after Wounds of the Head. Langenbeck's Arch. f. klin. Chir. XIII. Heft 3), to which my attention was not drawn until after the completion of this article, and wherein the etiology of hepatic abscesses is discussed in a very clear and comprehensive manner, there will be found (p. 586) a review of the occurrence and cause of hepatic abscesses, based upon the abundant material contained in the records of the Berlin Pathological Institute for the years 1859-1873. This synopsis is here quoted with the view of confirming and rendering more complete the statements above made.

Out of 7,326 autopsies, in 108 (*i. e.*, in 1.48 per cent.) hepatic abscesses and lesions of the liver were respectively found. These may be classified according to their etiology as follows:

Dilatation, ulceration of the bile-ducts	11
Diabetes mellitus	1
Phosphorus poisoning (areas of softening)	1
Unknown causes	5
Ulcerative processes in the tract of the *vena portæ*	18
Affection of the cæcum or processus vermiformis	8
Cancer of the stomach	5
Cancer of the pancreas	1
Cancer of the uterus and vagina	3
Fracture of the thigh	1
Gangrene of the lungs and pulmonary abscess	4
Injuries or inflammations of the external parts	55
Embolic form of pyæmia	30
(Head 7, other portions of the body, 22.)	
No appreciable embolic origin	25
Injuries of the liver	13
Healed ruptures	3
Unhealed ruptures (simultaneous injuries of the head, 2)	6
Direct wounds (head simultaneously injured, 1)	4
Total	108

As regards the especial frequency of hepatic abscess after injuries of the head, so often assumed, *Baerensprung* comes to the conclusion that this does not exist. Out of 33 cases of traumatic diseases resulting from injuries of the head and terminating fatally, hepatic abscesses were observed in 6, *i. e.*, 18 per cent.; out of 115 similar cases consecutive upon injuries, operations and phlegmons in other parts of the body, in 17, *i. e.*, in 15 per cent.

[2] Handbuch der historisch-geographischen Pathologie. Bd. 2, S. 300.

based upon a comprehensive study of the literature of the subject.

In those regions of Asia and Africa situated in the tropics, Upper Egypt and Algiers, the affection prevails as an endemic, constituting there as much as five per cent of all illnesses, and at times even a larger proportion. In the corresponding zones of America it is, upon the whole, of rare occurrence. In Europe it is found, again, to be relatively frequent in Andalusia, Malta, Sicily, and in the Ionian Islands; much more rarely in Portugal, Italy, and Turkey.

But within the tropics there are also certain regions which enjoy an entire, or nearly entire, immunity from this affection; such, for example, as the island of Singapore, also the south coast of China, the Sandwich Islands, and the continent of Australia. So, likewise, in relation to the occurrence of this disease, the case is very different with regard to many sub-tropical regions, notwithstanding their apparently similar climatic conditions; as, for instance, the provinces of Oran and Constantine, in Algiers; in the former it is very frequently observed, in the latter but seldom. The largest number of cases of endemic hepatitis occur usually, not in the hottest season of the year, but in that corresponding to our late summer and early autumn, which is characterized by the abrupt changes between the day-temperature, still quite high, and the night-temperature, relatively low. There are, however, exceptions to this rule: Rouis, in Algiers, and Jimenez,[1] in Mexico, saw most cases during the hottest months; Morehead, in India, during the cooler months.

The affection prevails in hot countries chiefly among Europeans and other foreigners residing there; whereas the natives, with the exception possibly of the blacks, are attacked far less frequently. To what this very striking predisposition of Europeans is due has not yet been accurately determined. Race alone does not appear to be the essential condition, for, as De Castro points out, in Egypt the European Israelites are quite as liable to the disease as other Europeans. In individuals who emigrate

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[1] *S. Pacheco*, Gaz. médic. de l'Algérie. 1871. Nr. 7. Jahresber. v. Virchow u. Hirsch für 1871. Bd. 2, S. 160.

from a temperate to a hot climate, the cause has been frequently referred to the alterations which the liver is said to undergo in consequence of this change of external influences (*vide* Hyperæmia of the Liver). This view is apparently corroborated by a communication of Rouis, according to which, in Algiers, during the years 1840–1856, the frequency of hepatitis was four times as great among North Europeans as among South Europeans. Additional proof was thought to be derived from the fact that, during residence in the tropics, the tendency to the disease at first increases, but subsequently diminishes; yet the statements of different authors as to the commencement of the influence of acclimatization read very differently according to the number of observations upon which individual opinions are based. Catteloup (20 cases in Algiers), De Castro (26 cases in Egypt), and Geddings (28 cases in India) set it at from two to four years; according to Rouis (131 cases in Algiers), the average in the army is at six, among the civilians at eight years; and McPherson's summary of 262 cases of hepatitis terminating in death, occurring within a period of five years among European troops in Bengal, no perceptible diminution in frequency can be recognized until the tenth year. It is, consequently, extremely improbable that the predisposition of Europeans depends upon conditions, the detrimental action of which is gradually weakened by acclimatization.

Much more plausible is the theory which, according to the estimate of Hirsch, is maintained by the great majority of medical observers in the tropics, viz., that the trouble is to be attributed chiefly to the improper diet which Europeans sojourning in those regions are accustomed to indulge in; for, instead of adopting a moderate and temperate regimen, and the food, chiefly vegetable, of the natives, they adhere to the rich animal fare to which they are accustomed at home, and the very frequent excessive use of spirituous liquors. The latter custom, especially, is almost universally regarded as a particularly active predisposing factor, and many (Cruwell, Henderson) discover, in the circumstance that the Asiatic people have remained almost entire strangers to this habit, an essential cause of the relative immunity enjoyed by them with reference to this affection.

Moreover, the dissimilarity above alluded to between North and South Europeans, as regards the frequency with which they are attacked, is perhaps accounted for in part by the predisposing influence of the abuse of alcoholic spirits.

Respecting other predisposing causes, we possess but meagre accounts, owing partly to the circumstance that our information is derived principally from material furnished by European armies. Rouis and De Castro, whose statistics relate to the civil population, lay stress upon the extreme rarity of the affection in the female sex; in the cases recorded by them, but 3.1 per cent. and 4.7 per cent., respectively, occurred in females. Moreover, of the eleven cases observed by L. Ramirez, one only was a woman. Age does not exercise any appreciable influence, except that the disease does not appear to occur at all during the first ten years of life. Unfavorable hygienic conditions and bodily hardships tend to increase materially this predisposition; which circumstance, according to De Castro, explains why comparatively more cases occur among the working-classes than among the well-to-do, and also why in Egypt, in the poor quarters, commonly occupied by Greeks, the percentage of hepatic abscess is almost double that found among all other European inhabitants.

In tropical regions a combination of hepatitis and dysentery is observed as occurring with remarkable frequency, though it is indeed possible—as has been maintained (and correctly, as it would appear) by Luchtmans, upon the strength of his observations[1] in the East Indies—that this frequency has been greatly over-estimated, diarrhœas produced solely by catarrh or simple follicular ulcers of the large intestine being often regarded as of a dysenteric character. There still remain, nevertheless, very

[1] These include 102 cases of hepatic abscess in which autopsies were held; of these there was found in 11 a normal intestinal canal; in 14, chronic catarrh of the large intestine; in 52, follicular ulcers in the colon; in 9, similar ulcers in the colon and ileum; and in 16, dysentery in various stages. Other authors, whose statistics are based upon observations made at the sick-bed, assign much higher figures to dysentery. *Rouis*, for instance, alleges that, of 143 patients with hepatic abscess, 128 suffered at the same time from dysentery, the symptoms of which had made their appearance in 80 cases before those of the hepatitis, in 25 simultaneously with the latter, whereas in 23 they were first observed during the course of the hepatitis.

numerous cases in which the results of the autopsy leave no doubt that purulent hepatitis and genuine dysentery have coexisted, or have immediately followed one another, in the same individual.

This complication of the two diseases has led to various hypotheses as to the mode of origin of tropical hepatitis. Budd favors the view that it is usually developed from dysentery as a secondary process; according to which theory, either pus or some other substance formed from the softened tissues, the fetid gases contained in the large intestine, or fluids from the intestinal roots of the portal vein, are reabsorbed and transferred with the blood to the liver, exciting there, either in scattered small areas, or in single large ones, inflammation and the formation of abscesses.[1] Bamberger, Tuengel, and Klebs also adopt the theory that the hepatic abscess of the tropics originates in emboli. That this view, however, is untenable may be learned from the following facts, made known chiefly by the writings of Frerichs and Hirsch: First, hepatitis is often met with in the tropics unattended by this intestinal affection; then, too, it often happens that the dysentery makes its appearance only after the hepatitis has been fully established. (Budd, with the view of harmonizing this latter fact with his theory, attempts to interpret it by assuming that the affection of the liver preceding the dysentery was not *suppurative hepatitis*, and yet when abscess-formation in the liver is subsequently found, this he considers to have been developed in consequence of the dysentery.) There are, furthermore, regions [Antilles, Cayenne] where dysentery is endemic in which hepatic abscess, at least among the natives [all India] when seriously attacked with dysentery, is very seldom, if ever, observed. Finally, all observers are agreed that, apart from the multiple hepatic abscesses which arise in the manner above described (p. 95) in exceptional chronic cases, suppurative hepatitis never supervenes in the epidemic dysentery of temperate climates, although this differs in no essential particular

[1] We will not here consider, inasmuch as it relates to the mode of production of dysentery, the opposite theory of *Annesley*, who attributes the dysenteric inflammation of the bowel to the irritation caused by the abnormal bile secreted by the diseased liver.

from that of the tropics.[1] Moreover, the relation of the two diseases to one another is by no means of such a character as to lend *à priori* probability to the theory of Budd; and this theory lacks, moreover, sufficient support from pathological anatomy; thus, there are recorded scarcely any observations of the existence of coagula in the veins proceeding from those parts of the bowels which are affected by dysentery; whereas in those cases in which an embolism conveyed through the portal vein forms the origin of the trouble, thrombi very often occur in the roots of this vessel (p. 93). Muehlig is the only writer who reports having found, in a case of hepatic abscess occurring after dysentery, small, yellow, apparently half broken-up coagula in the superior mesenteric vein. Furthermore, in the hepatitis of the tropics there is found in a decided majority of cases but a single abscess, whereas in that variety attributable to an aneurism of the portal vein quite a large number of purulent collections are quite as commonly met with. In a future chapter we will discuss the difference existing between the hepatic suppuration of the tropics and the metastatic variety, as regards the existence of fever.

However much we may incline to the opinion that there occur also in the tropical regions hepatic abscesses attributable to the same primary causes to which with us also the disease may, as a rule, be traced, an impartial consideration of the facts thus far elucidated must compel us in a majority of the cases there occurring to regard the suppurative hepatitis as an idiopathic disease; such, indeed, has been the experience of many writers, and especially of those whose observations have been made in warm countries.

Some of these writers, such as Bristowe, Dutroulau, St. H. Ward, have been led by the frequent coexistence of dysentery and hepatitis to adopt the view that both disorders are due pri-

[1] Thus, for instance, among the 231 autopsies of patients who had died of dysentery, which were made in Prague between February, 1846, and September, 1848, no single instance of abscess of the liver was found (*Finger*, Prager Vierteljahrschrift, Bd. 24, S. 145); and the same is true of the 80 cases of epidemic dysentery observed by *Niemeyer* in the Military Hospital at Nancy, in which an autopsy was made (*Burkhardt*, Berl. klin. Wochenschrift, 1872, Nr. 26).

marily to the same cause, and that it depends upon collateral circumstances and idiosyncrasies whether in one case one affection occurs, in a second case the other, or in a third both disorders appear simultaneously, or one shortly after the other. It must be acknowledged, however, that this theory fails to explain why, in the middle latitudes, the operation of this cause leads invariably to the production of dysentery alone, and never to hepatitis; in warm countries, then, some additional influence must be superadded, by virtue of which the poison of dysentery tends to frequently induce suppurative inflammation in the liver.

By other authors (Saunders, Annesley, Haspel) endemic hepatitis is assigned to the list of malarial diseases; a theory that is opposed, of course, by the fact that the disorder, as has been demonstrated by Hirsch, appears neither exclusively nor constantly in the malarial regions of the warm zone.

For the present the most comprehensive theory, and the one which corresponds most closely with the facts, is this: that in consequence of the deleterious influences, above described as predisposing factors—under which head are probably to be included also certain miasmata, such as malarial and dysenteric poisons—an irritation is first of all set up that assumes the form of hyperæmia, from which, the necessary causative influences being superadded, suppurative hepatitis is developed. Among such causative agencies are included sudden colds (Twining, Morehead, Murray, Catteloup) and the abuse of alcoholic liquors (Annesley, Heymann, and others). This explanation is manifestly superior to the theory of a miasmatic origin, in that it renders more easily explicable why the disease occurs especially among Europeans who have settled in warm climates, and why women are so very rarely attacked. As to the influence of sudden colds there is hardly room for doubt, for the evidence of numerous military surgeons shows that tropical hepatitis occurs most frequently in those seasons and regions in which a decided variation is observed between the temperature of the day and that of the night. Whether, however, the abuse of alcoholic liquors does not possess merely the significance of an important predisposing factor, constituting finally—to a certain extent by

virtue of its cumulative action—a direct cause of the disease, cannot be accurately determined from any observations thus far made.[1]

Pathology.

General Features of the Disease.

The clinical history of suppurative hepatitis presents such a complex variation that it is impossible to lay down any description of the symptoms which would be applicable in even a majority of cases. Its most perfect representation and one that, as regards its most marked features, is pretty constant, is met with in cases running a moderately acute course, to which belong many of traumatic and endemic origin. The affection begins here with symptoms of hyperæmic irritation of the liver, which may not unfrequently for a short time previous be preceded by, or accompanied with, gastric disturbances, pain in the region of the liver, and more frequently also in the right shoulder, increase in the volume of the liver, occasionally icterus, remittent fever of varied degree, coated tongue, anorexia, pain in frontal region, not seldom also vomiting, and usually sluggish, though at times

[1] In a work that has appeared since the completion of this article, "Ueber die Hepatitis der heissen Länder" [*The Hepatitis of Warm Climates*] (Arch. für klin. Chir., Bd. 19, Separatabdr., Berlin, 1876), *Sachs* represents it as very probable that in Cairo the hyperæmia of the liver, so easily developed under the influence of climate and irritative articles of food, is transformed into inflammation and abscess-formation. In support of this theory he appeals to the following facts: 1. Among the Mohammedan population of Egypt this disease is of extremely rare occurrence, and is then shown to appear only in individuals who, according to their own admission, have previously indulged in alcoholic liquors. 2. Of the thirty-six cases observed by him among the non-Mohammedan population of Cairo, composed about equally of both sexes, thirty-four occurred in men and only two in women; of the men the greater part were addicted to brandy, the others drank only wine, though occasionally slight quantities of liqueur; of the women one was devoted to the service of Bacchus. 3. According to the experience of *Sachs*, cirrhosis of the liver is of extremely rare occurrence in Cairo, while acute inflammations of the organ are, on the other hand, relatively frequent—a circumstance which he attempts to explain by the theory that alcohol, which gives rise in Europe to chronic interstitial hepatitis, induces, in like manner, in warm climates—where all vegetative processes run a more rapid and active course—acute purulent inflammation of the liver.

active, condition of the bowels: such are the appearances characterizing the first stage. When suppuration is established, the fever then assumes an intermittent type; attacks of chills, followed by heat and usually profuse perspiration, recur rhythmically or at irregular intervals; the tendency to pain and the enlargement of the liver increase; disturbances in the respiration supervene; frequently also a short dry cough; rarely hiccough. In case of a continuation of the gastric symptoms and the fever, which, when long protracted, may assume the character of *febris hectica* and diminish subsequently in intensity, nutrition and strength fail more or less rapidly. Moreover, if the suppuration continues restricted to the liver, there is not unfrequently superadded peritonitis or inflammation of the serous coverings of the thoracic organs. Should the abscess, however, extend beyond the boundaries of the liver, there then appear those symptoms dependent upon the lesions of the organs thus invaded. This results either in the formation of a circumscribed tumor of the abdomen or thoracic wall, which becomes gradually fluctuating and may ultimately open; or pus may be discharged by vomiting or with the fæces, or, preceded by signs of pneumonia, it may be coughed up; or there may be developed symptoms of a rapidly-formed exudation upon the right pleura or upon the pericardium, or those of a diffuse or encapsulated peritonitis.

It will now be evident, from the above brief sketch, that, as has been stated, the majority of cases exhibit more or less important deviations.

In metastatic hepatitis the ordinary symptoms of the first stage are, as a rule, wanting. The observation reported by Curschmann (loc. cit.) serves to illustrate, however, that the disease, when originating in a wound of the liver, may also remain quite latent until such time as the abscess is developed.

Where the affection runs an altogether acute course, there may be occasionally no other manifestations than severe fever with chills and serious cerebral symptoms, together with anorexia and constipation.

The absence of characteristic symptoms is much more frequently met with in chronic cases. Indeed, according to the state-

ment of trustworthy observers (compare Rouis, loc. cit., p. 101), in some instances of this class every sign of disease is wanting until, of a sudden, symptoms of the death agony make their appearance. At other times the disease runs its course under the form of a cachexia, either without fever or attended by hectic fever; the dependence of this cachexia upon some disorder of the liver is best betrayed by the abnormal sensations experienced in the vicinity of this organ. In other cases, again, the enlargement of the liver constitutes for a long while the sole symptom, the gastric disturbance and the gradual emaciation not appearing till later. It not unfrequently happens, moreover, that either the existence of the disease from which, or concurrently with which, the hepatitis is developed (pyæmia, dysentery), or else the symptoms which belong to the consecutive affections of the digestive and respiratory organs and their serous envelopes, completely mask, or force far to the background, the lesions attributable to the hepatic disorder. In the chronic variety the abscess, having long remained latent, may finally perforate a neighboring organ, and thus give rise to one or the other group of the symptoms above mentioned.

Where the result is fatal, the end usually approaches under symptoms of gradual exhaustion; less frequently with signs of peritonitis, exudative pericarditis, or some other accessory disease. In cases attended with fever occasionally brain-symptoms also ultimately supervene.

Should affairs take a favorable turn after the external opening of the abscess, then the fever disappears, the suffering of the patient abates, the discharge of pus becomes gradually less in quantity and finally ceases entirely, the liver returns after a while to its normal volume, bodily nutrition and strength are restored, and ultimately complete recovery usually ensues.

Anatomical Changes.

Suppurative hepatitis always appears in one or several isolated spots. Upon autopsy there are usually found fully-developed abscesses of an approximately globular form. If the disease is of metastatic origin quite a number of such abscesses

(as many as forty and upward) may be present; situated at times in adjacent groups, and at other times disseminated throughout the organ, and especially prominent in many cases upon the surface, where they form yellow, flattened projections. They generally vary in size from a hazel-nut to a walnut; rarely they attain the volume of a hen's-egg or goose-egg. In the traumatic, and especially in the tropical varieties of hepatic inflammation, there is usually found, on the other hand, a single abscess (according to Rouis, in North Africa, in 110 cases out of 146; according to Luchtmans, in the East Indies, in 65 out of 90; or according, therefore, to the combined calculations of both, in about three-fourths of all cases). The size of these isolated abscesses may be very considerable; most frequently they vary in volume between a man's fist and a child's head; but occasionally an entire lobe or the whole organ may be for the most part involved in the purulent cavity. In an observation reported by Rouis, an abscess extending throughout both lobes contained 4,500 grammes of pus, and was enclosed by a layer of hepatic tissue but one-half centimetre thick. This difference between idiopathic and metastatic hepatitis, as regards the number and size of the abscesses, is due mainly to the circumstance that in the former the duration of the disease is, as a rule, longer than in the latter. According to the statement of most writers, in warm climates the right lobe is attacked by inflammation with relatively greater frequency than the left, in a ratio corresponding to the difference in volume between the two lobes. Rouis, indeed, attempts to prove the contrary; but of the 127 cases contained in his table, in which the suppuration was limited to one lobe, 124 relate to the right lobe.

The mode of formation of hepatic abscesses has been made the subject of careful study, particularly in case of pyæmic deposits, inasmuch as the opportunity is here most frequently afforded of observing, side by side, the various stages of development. According to a description given some time ago by Virchow,[1] the process begins in the hepatic cells; certain acini,

[1] Beitr. zur experiment. Pathol. u. Physiol. Herausg. v. *Traube*. Heft 2, S. 62. Note, und Arch. f. pathol. Anat. Bd. 4, S. 314 f.—Compare also *A. Foerster*, Würzb. medic. Ztschr. Bd. 5, S. 43–47.

and subsequently smaller or larger groups of these acini, assume first a dirty yellowish-white hue, and later their central portion is found to undergo softening. Although such spots present, even at this stage, the exact appearance of abscesses, they nevertheless contain only opaque, coarsely-granular hepatic cells, and a mass of detritus arising from the disintegration of these cells, soluble, for the most part, in acetic acid; but as yet no trace of pus; suppuration is developed only as a secondary process, and at points that have undergone softening. Differing from this view, Frerichs (loc. cit., S. 97) and Klebs (Handb. der pathol. Anat., S. 429) describe the granular degeneration of the hepatic cells and the suppuration as forming simultaneous processes, although they, likewise, admit that the dissolution of the hepatic tissue thereby induced commences in the middle of the acini. The more recent observations of Klebs and Birch-Hirschfeld accord with the representation of Virchow, in so far as they affirm that pus-corpuscles are met with in the pyæmic deposit only after alterations in the hepatic cells have already taken place; these changes consist, however, not in granular degeneration, but rather in compression of the cells by the blood-capillaries filled with micrococci and greatly distended: while the walls of the capillaries and the hepatic cells are disappearing simultaneously with the very great multiplication of the micrococci, the suppuration begins upon the portal side of the acini.

According to the results of the experiments made by Koster[1] upon rabbits, in which inflammation of the liver had been excited by means of mechanical and thermic irritation, in traumatic hepatitis the process starts in the interlobular connective tissue. There is found in this tissue, around the vessels and in their walls, an immense aggregation of lymphoid corpuscles, which extend more or less between the rows of the hepatic cells; these cells themselves are at first well preserved, but in the peripheral portions of the acini, the intercellular (possibly lymph) spaces are everywhere distended and filled with coagulated, semi-transparent plasma and single, round cells; whereas in the vicinity of the central veins the swollen hepatic cells appear crowded

[1] Centralbl. f. d. medic. Wiss. 1868. Nr. 2.

together. Subsequently there supervenes purulent softening of the inflamed parts, which are then composed of the usual pus-corpuscles in addition to the products of the broken-up hepatic cells, of hepatic cells still well preserved, and fat-granules.[1] Quite similar is the process where the formation of hepatic abscesses is consecutive upon suppurative peripylephlebitis (compare R. Maier, l. c., S. 32 f.; A. Thierfelder, l. c., Fig. 2), and presumably, also, where it is occasioned by ulceration of the bile-ducts. The development of the abscesses in tropical hepatitis is not yet fully understood in its histological details; the earliest macroscopical changes consist here, likewise, in a pale-yellow coloration of certain groups of the hepatic lobules and in the appearance of miliary deposits of pus (Annesley, Haspel, Rouis). Rouis describes in the walls of larger abscesses actual holes, varying in size from a millet-seed to a pea, which contained in part pus and in part broken-down lobules.

Recent abscesses, formed in either of the modes just described, are usually filled with yellow, viscid pus; it often happens that their contents receive a brown or reddish tinge from the extravasated blood; and in cases where they are the result of ulcerated bile-ducts, a distinct bile-color may be observed. Their walls are rough and villous, owing to the presence of shreds of hepatic tissue of various sizes, which, infiltrated with pus, hang into the interior. The abscesses enlarge—apart from the increasing distention of the cavity from augmentation in the quantity of pus—by means of the progressive dissolution of their walls. Thus it frequently happens that adjacent abscesses become incorporated with one another, which will serve to explain the circumstance, that remains of former dividing septa traverse the cavity in form of a bridge or form radiating projections within it.

When the abscess reaches the surface of the liver, it then gives

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[1] *Froelich* (Untersuchungen zur Histologie der traumatischen Leberentzündung, Inaug.-Diss., Halle, 1874) found in the vicinity of silk threads, which he had drawn through the liver of rabbits—first, the parenchyma; then frequent and extensive streaks, dotted with a limited number of lymph-corpuscles and numerous globular bacteria, the latter of which were found at one point in and at another point between the hepatic cells; and subsequently cavities whose fluid contents consisted of pus-corpuscles and the remains of necrosed hepatic tissue.

rise to a circumscribed inflammation of the serous capsule, which often leads to gangrene of the affected portion with subsequent escape of pus into the abdominal cavity, and thereby to peritonitis, which is, as a rule, diffuse, though less frequently circumscribed by attachments. The inflamed portion of the hepatic capsule usually becomes adherent, however, to the superjacent abdominal wall or to a neighboring viscus, and when the suppuration then extends beyond the boundary of the liver, the result is that the abscess perforates the adherent organ. If the external abdominal wall is thus perforated, this part may be either penetrated directly outward, or the pus may seek an outlet by a circuitous route in the axillary, sacral, or inguinal region. If the abscess penetrates the diaphragm, purulent pericarditis may be the result; but far more frequently right empyema is produced; or, after adhesive inflammation between the diaphragm and the base of the lungs, ulcerative pneumonia supervenes, with a discharge of the pus into the bronchi. The colon, stomach, and duodenum are the principal abdominal viscera in which the perforation occurs; in very rare cases the abscess opens into the right kidney, and only exceptionally into the inferior vena cava and the portal vein; less seldom, on the other hand, into the gall-bladder and the bile-duct.

Those abscesses alone, as a rule, become healed which have discharged their contents externally, either directly or through the medium of another organ. The healing process is accomplished in the following way: the walls of the abscess cease suppurating, become more and more approximated, and ultimately are united by newly-formed connective tissue; from the contraction of this tissue there is produced in the parenchyma of the liver a radiating cicatrix composed of fibrous bands; and upon the outer surface a depression. In case the formation of pus is arrested without an evacuation of the abscess having previously taken place, the pus may become thickened by a resorption of its fluid constituents, while the cavity of the parenchyma becomes filled up by development of the interstitial tissue; the cicatrix then usually encloses a cheesy or calcareous mass. This mode of healing occurs, however, quite seldom, and, as a rule, only in case of small abscesses. The connective tissue thus developed usually

forms merely a capsule around the abscess, and the thickening of the pus is limited to the layer in contact with the walls which invest the smooth inner surface of the capsule like a membrane (so-called pyogenic membrane); the principal mass of the contents is still composed, as before, of liquid pus, which at times emits a pungent, ammoniacal odor. Abscesses may continue in this encapsulated condition for a long period; the capsule not unfrequently attains an almost cartilaginous consistence.

Of the larger blood-vessels, whose course lies in the neighborhood of an abscess, the hepatic veins are much more frequently affected by the inflammation than the twigs of the portal vein, probably because the latter are more protected by Glisson's capsule; the coagula in the inflamed vessels are found, for the most part, in a state of puriform dissolution. Obliterated arteries occasionally appear upon the walls of old abscesses in the form of cords and bands. It is only in exceptional cases that erosions of the vessels result from the progressive suppuration: bile-ducts, upon the other hand, are not unfrequently perforated by this process, though the quantity of bile escaping therefrom into the cavity of the abscess is often insufficient to produce any perceptible change of color in, or to dilute the pus.

In those portions of the liver not implicated in the inflammation, the parenchyma exhibits no constant alterations. Besides pyæmic abscesses, there usually exists diffuse granular degeneration. The general hyperæmia of the organ, such as is regarded by many authors as the first stage of acute hepatitis of warm regions, has not been observed in cases where a post-mortem examination demonstrated the existence of characteristic inflammatory deposits; though it is, indeed, true that recent, and especially rapidly-growing abscesses, not unfrequently are surrounded by a hyperæmic areola. In the vicinity of large collections of pus the hepatic tissue presents signs of compression, being paler and thicker, while the acini are diminished in size. And inasmuch as all abscesses, excepting those just beginning to form, usually occupy more space than those portions of the parenchyma from the dissolution of which they have been developed, the organ presents, therefore, for the most part, an increase in bulk, either limited to that part where a large ab-

scess is situated, or, in case numerous abscesses are present, general.

It is extremely seldom that gangrene is developed in the walls of the abscess. In abscesses that have burst, or that have been artificially opened, gangrene may be caused by decomposition of the pus induced by the entrance of air or of the contents of the stomach or intestine. In a case reported by Andral, of a man sixty years of age (loc. cit., Obs. 30), gangrene had been developed around an encysted abscess the size of an apple, the effect, probably, of extreme inanition due to a large gastric ulcer. Most observations respecting ichorous hepatic abscesses contained in the literature of the subject relate to metastatic gangrenous deposits transmitted from some peripheral part of the body, or from the lung, upon the margin of which a suppuration indicating the line of demarcation has supervened.

Symptomatology.

In the majority of cases *tumefaction of the liver* occurs; this may make its appearance frequently at the beginning of the suppurative stage, or during its subsequent course. The extent and form of the enlargement depends chiefly upon the number and situation of the abscesses, a certain influence being, of course, exerted by the condition of the remaining parenchyma; a more or less extensive hyperæmia of the gland is at the outset in many acute cases the only cause of, and may also continue subsequently to contribute to, the enlargement. Upon the contrary, in the chronic course, in consequence of secondary atrophy of the parenchyma, there may be no enlargement whatever even in case of extensive abscesses (*vide* Andral, loc. cit., Observ. 29). Slight degrees of enlargement can usually be detected only by the aid of percussion. If there exists considerable increase in volume in the right lobe, which may, as a rule, be recognized by decided bulging of the right hypochondrium, the dull sound may extend[1] upward by one or two intercostal spaces farther

[1] According to *Sachs* (loc. cit., S. 38) the rule is that the swelling occurs first in an upward direction, and subsequently downward.

than normal, or, what is more frequently the case, downward for a greater or less distance beyond the margin of the ribs. In exceptional instances enormous abscesses may produce a very considerable distention of the liver in all directions: Bitchey[1] reports a case where the right lobe was transformed into a cyst containing five quarts of pus; here the right half of the thorax, as far up as the apex of the lung, and the right side of the abdomen, as far down as the *crista ilei*, presented a uniform dulness. In extensive abscesses in the left lobe the tumefaction often extends over into the left hypochondrium below the navel, and even as far as the left ischiatic region; moreover, in consequence of the upward pressure of the diaphragm, the heart may be dislocated upward and to the left. The portions of the liver protruding from beneath the ribs exhibit an increased resistance, but never such a degree of hardness as in interstitial hepatitis. The lower margin admits often not only of being felt, but is also visible as a projecting edge. Inflamed parts which project upon the outer surface of any accessible portion of the organ may be distinguished at times upon palpation, at times also by the eye, as flattened prominences having less frequently the form of blunted cones. Such tumors are at first as large as a pigeon's or hen's egg, and firm or even hard to the touch; in their subsequent course they may grow to the size of the fist or larger, and present upon deep palpation a sensation of fluctuation, which, however, is usually obscure,[2] even when the condition of the abdominal parietes does not render its detection difficult. Abscesses which form a prominence upon the upper portion of the convex surface of the right lobe involve—provided they do not lie concealed directly beneath the vault of the diaphragm—a corresponding upward curvature of the superior line of hepatic

[1] Philadelphia Med. and Surg. Reporter. March, 1871. Schmidt's Jahrbb. Bd. 152, S. 260.

[2] An observation of *Sachs* (loc. cit., S. 36) demonstrates that such a circumscribed and obscurely fluctuating tumefaction in the hepatic region may also be produced by an abscess not situated in the immediately subjacent portion of the organ; here a large abscess, occupying the posterior surface of the liver, having found the ribs an insuperable obstacle to its growth backward, had pushed forward the entire softened part of the liver lying in front of it, and thus given rise to a prominence situated below the right margin of the ribs between the *linea parasternalis* and *linea papillaris*.

dulness that is otherwise straight; the highest portion of this line is situated upon the anterior surface of the thorax, sometimes nearer the sternum, at other times nearer the axilla, and in large abscesses may extend up even to the third rib. In such cases the upper margin of dulness constitutes a curve that bends upward toward the right from the sternum, descending abruptly in its course around the lateral wall and toward the spine.

If the hepatic swelling is quite considerable, it occasionally gives rise to a distention of the superficial veins in the region of the upper abdomen—obviously consecutive upon the pressure exercised by the swollen organ against the abdominal wall.

The tension of the right *rectus abdominalis* muscle, which was pointed out by Twining, first of all, as an important indication of a deep-seated area of inflammation in the right lobe, is due in all probability to a tonic reflex contraction. Bamberger, who regards this as a mere distention of the muscle from the enlarged liver lying beneath, appeals in support of this theory to his own experience, according to which this symptom in hepatic abscesses, as well as in other disorders of the liver, occurs only when associated with conspicuous enlargement of the organ. This tension is also observed, however—as is stated in the communications of Budd—in those affections of the bile-duct in which the liver undergoes no decided enlargement. Moreover, the circumstance that the change is limited to the right *rectus* seems to me to speak for its spasmodic character.

Pain in the hepatic region is one of the most constant of the local symptoms. It is absent most frequently in pyæmic hepatitis, and, furthermore, when the inflammatory deposit is very slowly developed, or when it is deep-seated. It often first makes its appearance when suppuration is beginning; or, if already present, it increases, as a rule, at this time; upon the other hand, after the development of the abscess it is wont to abate. So far as it is dependent upon inflammatory alterations of the parenchyma, it is only slight and dull; severer grades of pain are induced by affections of the hepatic capsule, caused either by its rapid distention in consequence of acute swelling of the organ, or, more frequently, as the result of an inflammation which, proceeding either from abscesses superficially seated, or from

those which have forced their way to the outer surface, implicates the serous covering. According to its quality, the pain is usually of a pressing or stretching character; less frequently tearing or pricking. Throbbing pain rarely seems indicative of abscess-formation; this symptom appears often to be induced, not so much by the hepatic abscesses, as by their projecting outward into the abdominal wall. In addition to the characteristic pain, the patient experiences at times the sensation as if a heavy body lay in the hypochondriac region, or as if a stick of wood were laid transversely across the upper abdominal region (*sensation de barre*). It often happens that the pain extends beyond the boundaries of the liver, shooting upward by irradiation more or less over the right half of the thorax, or less frequently downward in the direction of the abdomen, or even into the right thigh. The pain is usually restricted, however, to the hepatic region, involving either the whole of this region, or concentrated in a certain part of it. The latter point corresponds then pretty accurately, as a rule, to the seat of the inflammatory deposit; thus, in abscesses situated upon the posterior margin of the right lobe there is found, for instance, a circumscribed pain in the right lumbar region. Mechanical influences exerted upon the affected organ—such as may be excited by palpation, percussion in the hepatic region or pressure upon the same, by taking a long breath and coughing, and by changes in posture—tend to aggravate the pain, or, if it has not previously appeared spontaneously, to bring it on. In a case reported by Sistach,[1] the pain in the liver was excited only by riding on horseback. In traumatic and endemic hepatitis the region of the abscess may often be determined by a circumscribed tenderness upon deep pressure. In exceptional cases cutaneous hyperalgesia may be also observed at those points sensitive to deep pressure (Loewer). The pain may serve to determine the posture and attitude of the patient; if it is severe, the horizontal posture will be constantly maintained, the body being at times curved slightly toward the right, the thighs somewhat flexed, and the head inclined forward (Malcolmson, Dutroulau, Huet), a posture in which the pressure

[1] Rec. de mém. milit. 3. Sér. XX., p. 455.

upon the affected organ is reduced to the minimum:[1] if the enlargement of the liver, though considerable, is accompanied by but moderate pain, the patient usually lies upon the right side.

Pain in the shoulder, described even in the works of Hippocrates as a symptom of hepatic abscess, occurs[2] in about half the cases. It usually comes on shortly after, and less frequently simultaneously with, the pain in the liver; it may also appear, however, before the latter, or alternate with it; Cloetta, Habershon,[3] and Loewer relate instances in which, during the entire illness, or at least for a long period, it constituted the only indication of the existence of hepatic disease. It affects, as a rule, the region of the shoulder; it often extends, however, up the side of the neck, or backward over the shoulder-blade, or down the arm. Its situation upon the right side corresponds invariably to an inflammation in the right lobe, which then usually (but not, as Annesley alleged, without exception[4]) occupies the convex surface. It is extremely seldom that when the left lobe is affected, pain in the left shoulder is observed (for examples *vide* Gintrac,[5] Cas. Broussais, Muehlig). The abnormal sensation is described sometimes as of merely a dragging, stretching, or boring character, or, at other times, as a severe burning, shooting, or gnawing; it may be so intense that the pain in the liver assumes relatively a secondary importance. The pain in the shoulder may be aggravated by pressure in the hepatic region, and at times, also, by movements of the arms; by the former it is frequently excited temporarily in cases where it is not other-

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[1] *Sachs* (loc. cit., S. 35) maintains that in cases of very great intumescence of the liver, with perceptible widening of the intercostal spaces, patients occupying the horizontal posture are much more apt to incline toward the left than toward the right, and ascribes this to the circumstance that in bending toward the right the ribs are approximated, whereby an intolerable pressure is exerted upon the sensitive outer surface of the organ.

[2] This was observed by *Sachs* (loc. cit., S. 45) at least twenty-five times in thirty-six cases.

[3] Med. Times and Gazette. Nov. 4, 1865.

[4] Observation 32 of *Andral* affords an illustration of the existence of pain in the right shoulder accompanying an abscess situated close to the *inferior* surface of the right lobe.

[5] Journ. de la Soc. de Méd. de Bord. Juill., 1844.

wise present. Its duration is variable; frequently it only accompanies the development of the abscess; at other times it persists with fluctuating or almost uniform intensity for a period of months. In a case of hepatitis terminating in discharge of the abscess through the abdominal walls, Rouis observed that the deltoid muscle became atrophied after the disappearance of the shoulder pain. The most plausible explanation of this pain is that offered by Luschka,[1] that the filaments of the phrenic nerve which go to supply the serous capsule and the suspensory ligament of the liver (and under certain circumstances, also, the peritoneal covering of the diaphragm), when implicated in the inflammatory processes, transmit their abnormal irritation through the medium of the central organs to those filaments of the fourth cervical nerves that run across the shoulder, from which the phrenic nerve principally arises.

Icterus is one of the rarer symptoms. If a comparison is made of the statements of Morehead, Cas. Broussais, Rouis, Lyons, and Ward, respecting the frequency of its occurrence, it will be found that it is observed fifty-eight times in 375 cases; *i. e.*, in only about sixteen per cent. of the patients. Independently of a few cases running a very acute course, in which it appeared at an early stage as a symptom of general hyperæmia, and of such cases as are induced by or complicated with affections of the bile-ducts, it usually comes on at or after the commencement of the suppuration. As a rule, it continues slight, and persists but a short time. This mild and temporary icterus appears to arise most frequently from compression of the intrahepatic bile-ducts by purulent deposits. It is severer and more persistent when deposits exerting such a compression are developed in large numbers, or when a large abscess seated upon the concave surface of the liver presses upon the *ductus hepaticus* or *choledochus*. Excepting in these rare cases, it is not generally met with even when the pus-cavities are quite extensive. Where the abscesses are of pyæmic origin, it is often developed probably quite independently of the alterations in the

[1] Der Nervus phrenicus des Menschen, Tüb., 1853; und: Die Anatomie des Menschen, Tüb., 1863, Bd. I., Abth. 2, S. 221.

liver, inasmuch as the latter organ may in such cases be quite free from icterus, although the skin and conjunctiva are colored deep yellow, and the urine manifests unequivocally the reaction of bile-pigment, though containing no biliary acids.[1]

In many chronic cases, *fever* may apparently be absent during the entire course; at other times it supervenes simultaneously with the development or further extension of the abscess. Curschmann's observation, in which the first elevation of the temperature occurred thirteen days after the injury, shows that the fever may be wanting in the first stage of acute cases. As a rule, however, in acute hepatitis the fever appears much earlier or at the very outset of the disease. Detailed descriptions of the conditions existing previous to the formation of abscess are as yet wanting; in some reports of traumatic cases, however, mention is made of high persistent fever which appeared during the first days following the injury. On the other hand, more accurate observations are recorded in the publications of Traube, Tuengel, Wunderlich,[2] Kussmaul, Westermann, Heitler, Curschmann, and in the journals of the Rostock Clinique, which show that the various forms of fever may appear during the suppurative stage. The most characteristic form of fever is the regular intermittent, in which the attacks, ushered in by a chill and ending in a profuse perspiration, appear daily at about the same time, which is usually about evening. During the paroxysm of fever the temperature generally rises to 40° (104° F.) or even higher. In subacute cases this form of fever may persist for weeks. As Traube first pointed out, it is to be found only in cases where the abscess-formation in the liver is not caused by pyæmia, endocarditis, or pylephlebitis. Although in cases of hepatic abscess, due to the above-named causes, rigors of variable intensity and duration likewise occur, very frequently accompanied by profuse sweats, still these rigors always recur irregularly, appearing at quite variable intervals, sometimes of several days, sometimes occurring several times in a single day (as many as three or four times in twenty-four hours),

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[1] Vide *Leyden*, Beiträge zur Pathologie des Icterus. Berlin, 1866, S. 13.

[2] Archiv der Heilkunde. I., S. 25.

and only exceptionally recurring at the same hour for several successive days. The intervals are, moreover, never entirely free from fever, and the temperature sometimes rises as high as during the paroxysm, and, on the other hand, not unfrequently remains during the paroxysm below 40° (104° F.), although it sometimes rises above 41° (105.8° F.). (Comp. Tuengel, loc. cit., S. 170; Westermann.) Pyæmic fever of this kind may also occur in non-metastatic hepatitis and also in metastases of the lungs from hepatic abscesses (Curschmann). Thus are rendered explicable the cases in which at the beginning the paroxysms occur regularly or rhythmically at shorter or longer periods, but subsequently become irregular. In long-continued cases remittent fever with high temperature at night sometimes occurs, which, as the strength continues to diminish, passes over into the intermittent form by the fall of the morning temperature to or below the normal degree. In such cases the rapid elevation of temperature is not necessarily attended by a chill, but, on the other hand, profuse night-sweats are almost always present. If acute perihepatitis appears in cases running a short course, the fever assumes the continued form. The fever, if any there be, accompanying subacute and chronic cases, usually diminishes in intensity in the latter weeks of life; the average temperature is lower, and the rigors are absent. On the other hand, the pulse, which has hitherto stood in the ordinary relation to the temperature, is now continuously very rapid, so that even during the period of remission it far exceeds the normal rate, becomes progressively weaker, and frequently assumes an undulatory character.

As regards the fever in tropical hepatitis, information based upon frequent measurements of the temperature is wanting; still, it is at least certain, from the reports of observers in hot countries (Annesley, Haspel, Rouis, De Castro, *et al.*), that even in such localities the development and extension of hepatic abscesses are very frequently indicated by febrile attacks which present the closest resemblance to the paroxysms of malarial fever, both in the regularity of their recurrence and in the successive appearance of the cold, the hot, and the sweating stages. The fever generally assumes the quotidian type; not unfrequently that of the double quotidian; sometimes that of the

tertian or quartan; and occurs more frequently in the later hours of the day than at any other time. To be sure, the repetition of the attack on the same day might arouse suspicions that the fever was due to a pyæmic condition; but Rouis (loc. cit., p. 99) says positively, concerning the fever in the suppurative stage of chronic cases: "The attacks recur with perfect regularity [Ses accès sont d'une régularité parfaite]." If this statement is correct, the above-cited view of Traube, that recurrent fever, in the form of attacks returning at regular intervals, never appears in cases of hepatic abscess due to pylephlebitis, may be regarded as further evidence of the idiopathic character of tropical hepatitis. Rouis (loc. cit., p. 122), indeed, says, in another place, of the febrile attacks: "In some persons they obstinately retain their original type; in other cases they gradually approximate so as to acquire little by little the form of the double or triple quotidian, and even simulate remittent fever [Chez certaines personnes ils conservent opiniâtrement leur type originel; chez d'autres ils se rapprochent par degrés, au point d'acquérir peu à peu le type double ou triple quotidien, et même de simuler une fièvre rémittente];" but in these latter cases, which assume the doube or triple quotidian type, the attacks recur, in the beginning at least, with regularity. The irregularity which they present at a later period may be brought about by the formation of secondary abscesses, and possibly not only when these are formed in the lungs, but also when they appear in the liver itself. This hypothesis is based upon the fact that in the great majority of cases of tropical hepatitis (seventy-five per cent., according to Rouis) but a single abscess exists, and that, where several are found, one of them may generally be clearly demonstrated, by its size and other peculiarities, to be the oldest. It would surely appear admissible to regard the more recent abscesses as metastases which have originated from the older one, through the medium of thrombi in the twigs of the portal vein. (Comp. Klebs, Hdb. d. path. Anat., S. 429 ff.)

In hepatitis the *sleep* very generally presents anomalies; it is restless, disturbed by dreams, and unrefreshing, and frequently there is more or less complete insomnia. This latter is considered by medical observers in hot countries to be a characteristic

symptom of the disease, not to be accounted for by the physical suffering or mental perturbation of the invalid.

Grave *cerebral symptoms*—delirium, somnolence, forgetfulness, and the like—often appear toward the end of life, and now and then occur with severe fever in cases which recover. Sometimes these appear to be caused by gross anatomical alterations in the brain itself. In a case observed by Everett,[1] where the patient, thirty-eight years old, complained of headache two days before death, then fell into a condition of low delirium, and upon the last day went into violent convulsions, very numerous deposits of pus of varying size were detected in the substance as well as on the surface of the brain; while in the case reported by Faller,[2] where abscesses were discovered in various parts of the cerebrum and cerebellum, together with metastatic deposits in the lungs, no cerebral symptoms were observed.

Gastric symptoms—such as a thick, yellowish white coating on the tongue, the sensation of oppression and distention in the epigastrium, after eating; anorexia, oftentimes alternating with boulimia; vomiting of mucous or bilious matters;[3] constipation, or diarrhœa—are usually present in idiopathic hepatitis. Usually these are among the initial symptoms of the disease, and continue in acute cases during its entire course. In chronic cases these symptoms generally appear somewhat later, when the formation of the blood and the nutrition of the body have decidedly suffered in consequence of the long-continued suppurative process. The indications of acute or chronic catarrh of the mucosa of the digestive tract are often to be found in the cadaver; and, in tropical hepatitis, follicular or diphtheritic ulceration of the large intestine is very frequently seen; but in other cases these organs do not present gross alterations, or, at most, are merely anæmic. Thus, the stomach seldom appears perfectly normal when there has been obstinate vomiting during life, as has been remarked by Budd. Finlayson[4] and Grainger Stewart

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[1] London Gazette. May, 1847. [2] Ibidem. April, 1847.

[3] According to *Maclean* (Brit. Med. Jour., Aug., 1874; Virchow-Hirsch Jahresber., pro 1874, Bd. 2, S. 259), obstinate vomiting may be the only conspicuous symptom of abscesses existing in the substance or on the under side of the liver.

[4] Glasgow Med. Jour. Feb., 1873. Virchow-Hirsch Jahresber. 1873. II., S. 167.

each observed a case in which there were bloody discharges in the last days of life, without finding upon the post-mortem examination gross alterations in either the large or small intestine.

The *inflammation* of the serous capsule set up by superficial abscesses, which have not advanced to perforation, sometimes extends over the *entire peritoneum*, the exudation in such a case taking generally the sero-fibrinous form.

In patients who are very much reduced, *ascites* sometimes occurs as the symptom of general dropsy ; but it may be caused, as Haspel has observed, by compression of the portal vein by an abscess projecting from the under surface of the liver.

Hepatitis may in many ways give rise to abnormal appearances in the *respiratory organs ;* but these are often entirely wanting when the inflammatory deposit is centrally located and of moderate dimensions. If the liver is considerably enlarged, it hinders free motion of the diaphragm, and dyspnœa is caused by even slight physical exertion. Persistent difficulty of breathing comes on when a large abscess upon the convexity of the liver bulges up into the thorax ; still, the trouble is only moderate in degree, inasmuch as the contraction of the thoracic cavity takes place slowly. The compression of the lungs in this manner may be so considerable as to cause increase of the vocal fremitus and to give rise to an empty tympanitic sound in the upper part of the anterior wall of the thorax, as well as distention of the veins of the neck accompanying expiration (Immermann[1]). Extensive adhesions of the diaphragm to the liver and base of the lungs, ulcerative destruction of its musculature, and especially violent pain in the region of the liver, impede the diaphragmatic respiration so that the breathing becomes quicker and shorter, and assumes much more of the costal type. The dyspnœa caused by pain may be increased by external pressure upon the region of the liver, so as to cause a feeling of suffocation ; and a dry, distressing cough frequently accompanies this condition. The existence of this *tussis hepatica* may, as is maintained by Andral, have formerly been frequently assumed in cases where a complicating bronchitis was overlooked ; but Henoch goes de-

[1] Deutsches Archiv f. klin. Med. II., S. 354.

cidedly too far when he ventures to question its actual existence. When the inflammation attacks the diaphragm, irritation of the *pleura diaphragmatica* may be assumed as the cause of the cough. The cough, however, occurs also without any demonstrable affections of the air-passages, even when the suppurative deposits in the liver are far away from the convex surface. A case observed by Leyden[1]—in which a patient, suffering from colic caused by the passage of gall-stones, was several times attacked by a dry cough, with pain in the right hypochondrium, twenty-four hours before the paroxysm, the cough ceasing upon the appearance of icterus—makes it seem probable that a cough may be due to the condition of the liver.

Still more obscure as regards its mode of origin is *singultus*, which appears in quite exceptional instances long before the commencement of the death agony, and is usually in such cases extremely obstinate.

The results which follow perforation of the thorax by an hepatic abscess will be considered presently; it may be mentioned, at this point, however, that hepatitis sometimes causes considerable disturbances in the respiratory organs, inasmuch as the inflammatory centres in contact with the diaphragm set up, even without perforation, an acute *pleuritis* with sero-fibrinous exudation. In like manner, *pericarditis* may also be induced by propagation of the inflammatory process in the liver, without destruction of the diaphragm.

In cases in which fever and icterus are present, the *urine* manifests the changes resulting from these conditions, and, when the fever is high, is not unfrequently albuminous. The urine exhibits nothing characteristic of the disease, except the abnormal ingredients which may appear in it in consequence of the extremely uncommon event of the perforation of the pelvis of the right kidney by an hepatic abscess. (See below.)

Suppurative hepatitis exerts, of itself, no appreciable influence upon the *spleen*. The traumatic and idiopathic cases, with violent fever, are only occasionally accompanied by enlargement of the spleen; while, on the other hand, in hepatitis due to pyæmia

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[1] *Kohts*, Virchow's Archiv. Bd. 60, S. 199.

and pylephlebitis it is invariably present. When the hepatitis is complicated with dysentery, the spleen is usually small; when in tropical hepatitis it is found large and solid, this condition is usually due to malarial complications. In long-continued suppuration in the liver, enlargement of the spleen, caused by amyloid degeneration, sometimes takes place

The *nutrition* is most notably affected in the subacute and chronic cases attended by fever, decided emaciation seldom appearing in very acute cases; while in the feverless chronic hepatitis a moderate or even considerable amount of strength is kept up, and there may even be, as Rouis observed in three cases, an increase of the subcutaneous adipose tissue, commencing during the course of the disease, and continuing until death. As a rule, however, the patient gradually declines, becomes paler and weaker, and frequently at the last dropsical. In the endemic form of hepatitis, the skin often displays a cachectic coloration, which by some observers is compared to the color of damaged wax.[1]

There remain to be described the symptoms caused by the *perforation of the hepatic abscess* in the various above-mentioned directions. In perforation of the *external walls* there is formed in the epigastrium, right hypochondrium, right lumbar region, or one of the lower intercostal spaces, a flat tumor, which increases slowly, and is generally very sensitive to pressure. After a while (two or three weeks, Rouis), fluctuation may be detected. The surrounding tissue is generally odematous, and the doughy condition of the tumor itself is often such as to hinder or entirely prevent the discovery of fluctuation. After the skin at the apex of the tumor has reddened and become covered with blisters, it finally bursts and lets out the contents of the abscess. Sometimes, after the fascia and muscles of the abdomen or the thorax are perforated, a sharply-defined prominence appears at the corresponding cutaneous surface, which may be made to disappear like a hernia. Some observers have seen, in very rare cases, the occurrence of gangrene of the abdominal wall over the

[1] *Sachs* (loc. cit., S. 32) describes the appearance of the sclerotica in hepatic suppuration, which may be compared in color and sheen to partially bleached wax, as a characteristic symptom of the disease.

whole extent of the tumor, as well as necrosis of the lower ribs. In exceptional cases the pus burrows between the layers of the abdominal or thoracic wall for a considerable distance, and finally comes to the surface, for the first time, in the axilla, near the last lumbar vertebra, upon the hip, in the inguinal region, or even on the inner surface of the thigh. In a case described by Rouis, the pus made its way between the layers of the ligamentum suspensorium to the navel, through which it was evacuated.

The opening of an hepatic abscess into the *stomach* is often preceded for a long time by symptoms of dyspepsia, frequently also by a feeling of oppression experienced after each meal, or, as in Koehler's[1] case, by severe attacks of dyspnœa. When the perforation takes place, a considerable quantity (several hundred c. ctm.) of more or less fetid pus is usually vomited up at once. The vomiting of lesser amounts of pus may be repeated for successive days. The stools, too, frequently contain pus, but are seldom made up entirely of it. The hepatic tumor diminishes in size, and the more copious the discharge of pus the more rapidly do the secondary disorders disappear. In the cases observed by Graves[2] and Tophoff,[3] immediately after the vomiting the former dulness over the tumor was replaced by a clear tympanitic sound upon percussion.

When the abscess opens into the *colon*, there then appears in the stools a considerable quantity of pus, which, according to Heinemann, is of a brick-red color. Sometimes this perforation manifests itself by the occurrence of sudden acute pains in the abdomen, or, as in v. Franque's[4] patient, by the sensation that something has given way inside the body.

When the contents of the abscess are evacuated into the *duodenum*, either directly or through the gall-duct, after perforation of the latter, reddish pus may appear in the stools as well as in vomited matters.[5] When the pus all passes downward

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[1] Deutsche Klinik. 1864. Nr. 36 und 37.

[2] Dublin Jour. Jan., 1839.

[3] Ueber Leberabscess. Inaug.-Diss. Halle, 1874.

[4] Memorabilien. XI., 1. 1866.

[5] As in a case related by *Jubiot* (Le mouvement médic., 1873, Nr. 49), where the pus passed into the duodenum from the gall-bladder, which was implicated in the abscess.

through the intestine, it is frequently mixed so intimately with the fæces as to be difficult of detection. In such cases a probable diagnosis is all that can be made, and this rests upon the coincidence of the sudden feeling of relief, with the appearance of the diarrhœa, and the rapid disappearance of the objective symptoms.

When the abscess opens into the pelvis of the right *kidney*, the pus is evacuated with the urine. In the case reported by Huet[1] the urine, voided with tenesmus, after having been bloody for several days, showed a dirty brown coloration, and yielded a copious deposit, containing, along with pus and red blood-corpuscles, a great number of liver-cells. This condition gradually changed, disappearing entirely at the end of several weeks, while during this time normal, pale, clear urine (from the left kidney, the right ureter being occluded) was passed but once. After the liver, which before was very much smaller, had returned to its normal size, the region of the right kidney showed an increased sensitiveness to pressure, the pain shooting down toward the bladder and the right inguinal region.

When the abscess makes its way into the *bronchi*, indications of an inflammatory infiltration in the lowest segment of the right lung soon appear; a marked dulness extends for several finger-breadths upward from the base of the lung, and less frequently reaching to the scapula; auscultation reveals crepitant râles or bronchial breathing; and, in addition, more or less acute pain in the shoulder, difficult breathing, and cough, with sputa typical of pneumonia or catarrh, are present. In a case which came under my own observation the accompanying fever was intermittent (temperature rising in the evening to 39.7° (103.5° F.), and falling in the morning some tenths below 37° (98.6° F.). After the dyspnœa and frequency of the cough has increased, and the breath (as often happens) has become offensive, the sputum changes its character. At times there is suddenly thrown out—generally with violent choking—a torrent of pus of a reddish brown, brick-red, or yellow color, having a putrid odor and taste. The quantity of this pus may be very abundant. In Heaton's[2] case it

[1] Nederl. Tydschr. voor Geneesk. 1867. I., p. 648.

[2] Brit. Med. Jour. July 3, 1869.

formed in six hours sufficient to fill a chamber-vessel. At other times the sputum consists of thick lumps, in which streaks of whitish or reddish brown pus are cemented by means of viscid mucus, blood being frequently present, and, as Rouis (loc. cit., p. 138 and p. 184) has shown, shreds of tissue from the lungs, or possibly the liver, may occasionally be included in the expectoration. According to Heinemann the clear brick-red color of the purulent expectoration is so characteristic that it is sufficient in itself to determine the diagnosis of hepatic abscess. Budd also, in several cases, based the diagnosis of hepatic abscess, of which he had had no previous intimation, upon the color of the expectoration. According to this latter writer, the pus first takes on this peculiar color during its passage through the lung, in which it is mixed with blood and broken-down parenchyma. Still, as Rouis suggests, it is quite probable that the pus contains the coloring matter (altered hæmoglobin) before leaving the liver, inasmuch as the contents of the abscess evacuated through the abdominal wall, or detected post-mortem, is found colored different shades of red. Frequently bile is found along with the pus in the expectoration. (In one of my cases—demonstrated by Pettenkofer's test—the bile appeared from the second day, continuing present for three weeks, and for months in two of Heinemann's cases, which, like mine, terminated in recovery.) Pure bile is also often coughed up in large amounts, one of Rouis's patients raising 900 grammes in two days, while in a case in Hasse's clinique, reported by Wolfes,[1] 400 c. ctms. of a yellowish fluid were expectorated, which contained bile-pigment and liver-cells, some of which were perfectly preserved, while others were partially broken down. Heitler saw greenish yellow sputa, containing bile-pigment, but no biliary acids, precede for several days the expectoration of pus. Air which has passed from the bronchi into the purulent deposit of the lung may, when the latter is favorably situated, give upon percussion the indications of a cavity within the area of dulness corresponding to this deposit.

If the perforation of the diaphragm is into the right *pleura*—which, although very infrequent, may even occur in case of

[1] Deutsche Klinik. 1864. S. 11.

abscess of the left lobe (Peacock[1])—the symptoms of a rapidly developing empyema appear. In such case no diminution of the volume of the enlarged liver is to be demonstrated; on the contrary, the lower edge of this organ reaches lower down, and above, the dulness of the liver passes directly over into that caused by the fluid contents of the pleura. The possibility of distinguishing such a condition from a pleuritic exudation, caused, without previous perforation of the diaphragm, by an abscess upon the convexity of the liver, is greatly reduced, inasmuch as it is highly probable that such an exudation already exists before the upper layer of the diaphragm is completely perforated by the ulceration. The conclusion that the perforation has taken place is apparently correct when, at a later time, the puriform character of the contents of the pleura is demonstrated by its discharge through the wall of the thorax or into the lung and the bronchi. For the cases, like that observed at Traube's clinique by Loewer,[2] are extremely rare in which, without perforation of the diaphragm, pyothorax is developed, and opens through the bronchi.

The discharge of pus from the liver into the *pericardium* causes pain of more or less severity in the cardiac region, irregular action of the heart, palpitation, anxiety, a sensation of oppression, and suffocation, as well as the physical indications of a rapidly increasing pericardial exudation. In a case in which the abscess opened into both the stomach and the pericardium, Graves[3] detected a metallic tinkle accompanying the heart-sounds.

When the abscess opens into the *abdominal cavity*, the symptoms of diffuse peritonitis generally follow. In rare cases, however, when the pus is discharged slowly, or when sufficient adhesions have been previously formed around the place of perforation, the indications of peritonitis remain limited to a circumscribed area, an encysted pus-deposit being formed. This deposit may then open outward through the abdominal wall, as

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[1] Transact. of the Pathological Soc. XIX., p. 243.

[2] Berl. klin. Wochenschrift. 1864. S. 461.

[3] Dub. Jour. Jan., 1869.

occurred in a case of Cambay (loc. cit., p. 225) between the eleventh and twelfth ribs, or in that of Rouis (loc. cit., p. 319), in which there occurred a perforation from the liver into the great omentum and subsequently through the epigastrium; or it may communicate with the colon, as in the cases reported by Schmidt and Koster,[1] and by Domenichetti,[2] where a distinctly fluctuating tumor existed in the one instance between the ensiform cartilage and left ribs, in the other behind on the right side over the two lower ribs, in which the contained air could be demonstrated by palpation and percussion. Haspel (loc. cit., p. 193) mentions the case of a patient in whom an encysted pus-deposit extended from the liver to the inguinal canal, and the pus pouring into the latter formed an extensive tumor reaching down into the scrotum. Kallies[3] reports an exactly similar case, in which puncture of the scrotum caused the discharge of a very great amount of pus, and was followed by recovery.

Perforation of the *portal vein* by an abscess situated in the left lobe occurred in a case described by Wyss, without giving rise during life to any symptoms pointing to this process. The same is true of a case of Colin,[5] in which the abscess communicated with the *vena cava* by an opening twenty-five millimetres in diameter.

Perforation occurs in about one-half of the cases of hepatic abscess. Of the 203 cases collected by Rouis, the suppuration spread beyond the liver in 107, and in 17 of these, where several abscesses existed, only a part opened spontaneously. The following numbers will show the relative frequency of the occurrence of the perforation in the several directions: of 170 cases, 24 of which are taken from the latest literature, the others from collections of Rouis, Dutroulau and De Castro, the perforation in 74 was into the bronchi, in 32 into the intestinal tube, in 26 into the right pleura, in 23 into the abdominal cavity, in 13 into the stomach, in 4 into the pericardium, in one into the pelvis of the

[1] Neederl. Weekbl. Juli, 1854. Schmidt's Jahrbb. Bd. 88, S. 310.

[2] The Lancet. 1863, 6 February. A similar case is also mentioned by Bristowe (l. c.).

[3] Med. Zeit. Russl. 1845. Nr. 6 u. 7.

[4] Wiener medic. Presse. 1865. Nr. 50 u. 51.

[5] Gaz. hebdom. de méd. et de chir. 1873. Nr. 33.

right kidney. No estimate can be given with regard to the perforation of the abdominal wall, inasmuch as the cases in which this process took place spontaneously cannot well be separated from those in which it was brought about or aided by artificial means.

Among the above 170 cases there are three in which successive perforations took place in different directions. Whether such openings originate in the same or different abscesses, can hardly be determined with certainty during life. The latter case is the more probable when one of the organs invaded by the suppuration is upon the concave, and the other upon the convex surface of the liver, as, *e. g.*, when the perforation takes place in the pleura and the peritoneum (Haspel, loc. cit., p. 182), or in the bronchi and the intestine (Depesselche[1]); while two perforations communicating with the same abscess are to be found, as a general rule, upon the same side of the liver, as in Budd's case (loc. cit., p. 86), in which first the stomach and then the abdominal wall were perforated, and in that of Marroin,[2] where the pus burst into the pleura and the seat of the kidney. When, however, the abscess occupies the entire thickness of the liver, the perforation may be in exactly opposite directions, as, *e. g.*, into the colon and the pericardium.[3]

Complications.

Apart from the dysentery and malarial fevers of hot regions, there is no disease—if consecutive inflammation of the peritoneum and right pleura be excepted—which occurs with any relative frequency as a complication of suppurative hepatitis. Sometimes pericarditis and pleuritis, both usually accompanied by sero-fibrinous exudation, as well as pneumonia, supervene, when the centre of hepatic inflammation is not seated near either the pericardium or the pleura, and are usually, in such cases, the proximate cause of death. Moreover, the changes in the liver itself, as well as in other organs, due to chronic alcoholism—fur-

[1] Jour. de médec. 1843, Juillet.

[2] Arch. génér. 5. Sér., T. XX., p. 568.

[3] Ibid., 1828, p. 98.

thermore, chronic affections of the lungs and bronchi, chronic hepatitis, pyelitis, etc.—occasionally accompany hepatic abscesses, and hasten the exhaustion of the invalid. In quite exceptional cases *erysipelas capitis* (Andral, Observ. 28), bilateral suppurative parotitis (Koehler, l. c.), and thrombosis of the femoral vein (Jefferson and Martin[1]) have been observed as accessory diseases.

Diagnosis.

Cases are not infrequent in which it is impossible to recognize the disease during life, either because of the absence of all symptoms indicating liver disease, or because of the presence of only those symptoms which cannot be traced with certainty to the liver (*e. g.*, pain in the shoulder), or which may be equally due to some other disease of that organ (such as hypertrophy, icterus, etc.). To this category belong especially chronic cases ; and, above all, such as occur concomitantly with, or in the train of, other diseases whose symptoms accord with those induced by suppurative hepatitis ; so also cases complicated with dysentery occurring in warm climates, and many cases appearing with us as an accompaniment of pyæmia, as well as some others proceeding from affections of the gall-ducts. Among these are to be reckoned, furthermore, many insidiously progressing cases which come under observation only when the suppurative process extending beyond the borders of the liver sets up inflammatory changes in other neighboring organs ; the latter alterations are then readily taken for independent affections, inasmuch as the clinical history frequently furnishes no clue to the original disease. This remark is applicable to the consecutive pleuritis and the disturbances induced by the perforation of the lungs, especially when such disorders persist for a long time, and are accompanied by a chronic bronchitis, to which the purulent expectoration can be referred ; as, for example, in one of the cases reported by Kussmaul. Heinemann remarks concerning the diagnosis of tropical hepatitis : "Diseases of the lower lobe of the right lung must be studied with great care, in order to determine as to the

[1] The Lancet. 1860, Feb. 7.

presence of an hepatic abscess." In a case related by Dohlhoff,[1] in which perforation of the pelvis of the right kidney took place, the patient suffered, during the last eighteen months of his life, from attacks of pyelitis.

But even when the disease gives rise, from the beginning, to more distinct symptoms, the diagnosis does not, as a rule, become certain until the symptoms of abscess-formation (rigors, projections upon the liver which may be felt or percussed, fluctuation) have appeared. The only exception to this rule is to be found in the cases in which one of the causal factors of suppurative hepatitis is present, whereby the theory of the existence of the disease may be rendered *à priori* probable. Hence, in regions where the disease is endemic, the symptoms of the first stage (gastric disturbances, fever, painful enlargement of the liver, pain in the shoulder, sleeplessness) possess pathognomonic importance. Among us the traumatic cases are the ones which often permit of an early and direct diagnosis. In all other cases the correct conclusion is usually reached much later by the roundabout process of elimination, which, strictly speaking, affords, often enough, nothing but a scientifically-grounded conjecture.

The difficulty of diagnosis is shown most conspicuously in that, even when considering such symptoms as are most characteristic of suppurative hepatitis, this may be confounded with other diseases if the observations are not made with great care. Whenever fluctuation can be felt in a circumscribed area in the region of the enlarged liver, there is generally but little doubt concerning the nature of the disease; and yet, with regard to these symptoms, error is not impossible.

Echinococcus cysts are hardly to be mistaken for abscesses, inasmuch as their development is slower, usually painless, and is not followed by any injurious effects upon the nutrition of the body; while, on the other hand, the suppuration of an echinococcus cyst produces the same symptoms as does an hepatic abscess, so that it is only by a knowledge of the previous symptoms that the two can be with certainty distinguished from each other.

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[1] Med. Zeit. des Vereins f. Heilk. in Preussen. 1837. Nr. 38.

Distention of the gall-bladder, which shows some similarity to an abscess in the neighborhood of the gall-bladder, by presenting a painful fluctuating tumor at the edge of the liver, and by an accompanying fever which is often attended with chills, may generally be distinguished, upon more careful examination, by its pear-shaped or semi-globular form, the abscess having the shape of a low, rounded prominence, with a broader base. The doughy feeling which is usually observed in hepatic abscesses adherent to the abdominal wall, is wanting to the swollen gall-bladder.

In cases of medullary cancer of the liver, when, as exceptionally occurs, the superficial nodules are so soft as to give fluctuation, mistakes can be avoided only by a careful consideration of all other circumstances of the case.

In order to distinguish between an abscess in the deeper layers of the abdominal wall and an hepatic abscess which may be suggested by the position of the former, Sachs[1] (Cairo) recommends that a fine insect-pin be thrust into the tumor until the cessation of resistance indicates that the cavity is reached, when, if it is an hepatic abscess, the free end will move in the opposite direction to the motion of the diaphragm, remaining, on the other hand, motionless during respiration when inserted in an abscess of the abdominal wall.

Rigors, which are so important in the diagnosis of suppurative hepatitis, may also be as misleading as fluctuation. When these recur with regularity, followed by the hot and sweating stages, with intervals of freedom from fever, they frequently lead to the diagnosis of intermittent malarial fever, but are to be distinguished from the paroxysms of the latter in that they almost always appear in the afternoon or evening, and are only slightly, or not at all, controllable by quinine; while the malarial attacks usually occur between midnight and noon. (The contrary observations of Cambay and Jaccoud[2] upon the efficacy of quinine remain wholly unconfirmed.) It should be added that any demonstrable enlargement of the spleen is also frequently

[1] Gaz. hebdom., 1868, No. 14; Ueber Hepatitis der heissen Länder, Berlin, 1876, S. 71 f.

[2] *Dieulafoy*, Gaz. des Hôp. 1867, 89.

wanting, while the liver is usually swollen more than in ordinary malarial fever.

Rigors and elevations of temperature, recurring irregularly in connection with icterus and moderate enlargement of the liver, also occur in those cases of pyæmia in which the liver remains free from metastases. Even when a peritoneal pus-deposit, or a pre-existing ulceration in the tract of the roots of the portal vein can be demonstrated, the above-mentioned symptoms do not yet justify the positive diagnosis of hepatic abscess, as these may be due to a pylephlebitis which has not extended into the parenchyma of the liver. Under such conditions, a well-marked sensitiveness of the liver is the most valuable diagnostic sign.

Irritation of the bile-ducts by calculi also gives rise sometimes to febrile attacks, which begin with rigors and recur at regular intervals; while pain in the region of the liver and even in the shoulder and lumbar region, as well as gastric disturbances, may also be present, so as to present a group of symptoms very similar to those of hepatitis with abscess-formation. However, not only is the splenic enlargement which accompanies metastatic hepatitis wanting, but the liver, as a rule, is of normal size, and, when enlarged by a stasis of bile in consequence of occlusion of its duct by a calculus, icterus is present of such a degree of intensity as is only occasionally to be seen in hepatic abscess—apart from the very rare cases in which the *ductus choledochus* is compressed by the abscess itself—caused by inflammation of the biliary passages due to the presence of calculi.

In many chronic cases of hepatic abscess in which hectic fever and night-sweats are present, together with moderate enlargement of the liver, the complication of chronic bronchial catarrh may easily lead to its being mistaken for pulmonary phthisis, which error may, however, be always avoided by careful consideration of the history of the case and by accurate observation of the condition of the apices of the lungs.

The best protection against the error of attributing the changes in the physical condition of the thorax, caused by a large abscess on the convex surface of the liver, to pleuritic exudation, consists in accurately noting the upper limit of dul-

ness. This always rises higher, in such abscesses, upon the anterior wall of the thorax than upon the back (*vide* above); while it is well known that in pleuritic exudation the contrary condition generally exists, or, at any rate, the line runs at the same level around the affected side.

Course, Duration, Termination, Prognosis.

In the majority of cases suppurative hepatitis assumes a chronic form; and, even where it begins with acute symptoms, the suppurative stage is often of long duration. If the affection runs an acute course throughout, it exhibits a uniform progress also in its symptoms. In the subacute and chronic cases it often happens that some, and perhaps the greater part, of the symptoms are temporarily modified, or disappear altogether, to become aggravated again, or to reappear anew, at the expiration of weeks or months. There may be, also, occasionally interposed during its progress a period of complete latency.

As regards the duration great variations are manifested. In traumatic cases, where this can be most accurately determined, it varies, where the result is fatal, between several weeks (twenty-five days, Curschmann) and two years (Andral, Observ. 28); where the disease terminates in recovery, it usually lasts from two to three months, though the duration may also be somewhat shorter, or, again, much longer. A railway servant, in whom a fluctuating tumor, seated at the margin of the ribs, was laid open by Fischer[1] by means of an incision, twenty days after the reception of the injury (blow from a railway-wagon in the region of the liver), was able to resume work by the seventh week. In a case observed by Goodwin,[2] in a delicately-formed woman, where spontaneous opening into the stomach, and subsequently through the abdominal wall occurred, a fistula still remained open ten months after the injury. Among the idiopathic cases some are observed, in tropical as well as in temperate regions, which, after a course lasting but from one and one-half to three

[1] Zeitschr. f. Wundärzte und Geburtsh. XXI., 2, S. 81.

[2] Brit. Med. Jour. Sept., 1864.

weeks, terminate fatally. According to Dutroulau, the disease may run through all its stages in from eight to ten days. Rouis states that the shortest duration in cases complicated with dysentery is ten days; in cases not so complicated, eighteen days. In one of the cases reported by Andral (loc. cit., p. 75), death supervened at the expiration of seventeen days; in another case of the same author (Observ. 22), at the expiration of fourteen days; in the case communicated by Wunderlich,[1] as early as the twelfth day.

It is usual, however, for the disease to extend over a much longer period, which very often cannot be accurately determined, either because the beginning of the process is too slightly marked, the symptoms not being well defined until suppuration has commenced, or because the hepatitis remains quite latent up to the time of the appearance of the phenomena indicating perforation into a neighboring organ. Reckoning from the first symptom of the disease to its termination in death or in recovery, there will be observed in a majority of cases a duration of from one to five months. In the six cases induced by embolism of the portal vein, reported by Tuengel, from 27 to 38 days intervened between the appearance of the first chill and death. According to the observations of Geddes (in Madras), the average duration amounted to between 40 and 118 days. Of 192 fatal cases, Rouis observed that, where the abscesses did not open externally, the duration was, on the average, 70 days; where they resulted in perforation, 110 days; and in 26 cases terminating in recovery, where they discharged their contents externally, 140 days. The longest duration reported by Rouis, in a case complicated with dysentery, where the abscess remained confined, amounted to almost sixteen months. There may be found isolated statements according to which the disease may apparently last a much longer period. An observation of this kind by Andral (death two years after the injury) has been already quoted. In a case reported by Mayet[2] death supervened after an illness of two and one-half years, dispersed, however, with intervals of relief lasting months. Greenhow[3] relates the

[1] Arch. d. Heilk. I., S. 25. [2] Gaz. hebdomad. 1873. Nr. 39.
[3] Transact. of the Patholog. Soc. XVIII., p. 117.

case of a man, aged sixty-two years, who, after a residence of thirty-five years in India, had experienced during the subsequent six years in England various attacks of fever accompanied by non-rhythmical, recurrent chills, and had gradually acquired a tumor of considerable size: on post-mortem examination there was found in the left lobe one very large abscess and several small ones, and upon the hypertrophied right lobe a cicatrix penetrating deep into the texture. In the case of Lawson, the surgeon, who had survived an acute hepatitis occurring in India more than ten years previous to his death, the liver contained (as is reported by Budd, loc. cit., S. 165), in addition to a stellated cicatrix of the consistence of cartilage, numerous abscesses each as large as a hazel-nut and filled with white pus. Bertulus[1] reports a case where the hepatitis is said to have lasted as long as fifteen years.

Suppurative hepatitis *terminates* much more frequently in *death* than in recovery. In the endemic form in North Africa there occurs upon the average one case of recovery to four fatal cases (in Algiers, according to Rouis, 162 died out of 201, *i. e.*, 80 per cent.; according to statistics gathered by the Medico-Chirurgical Society of Alexandria, 58 out of 72, *i. e.*, 80.55 per cent.; according to De Castro, of Alexandria, 93 out of 128, *i. e.*, 72.55 per cent.). In the East Indies, according to the statement of Morehead, the proportion appears to be far more favorable; among those admitted to the hospitals suffering from acute or chronic hepatitis, the above-mentioned author found a mortality of only 14 to 37 per cent.; he himself admits, however, that cases of cirrhosis may have been included among his statistics; it should be added, moreover, that among physicians practising in the tropical regions, acute hyperæmia is usually regarded as the first stage of hepatitis. The observations above quoted respecting Africa relate, however, exclusively to cases in which suppuration supervened. The frequency of the fatal termination in those regions is attributable chiefly to the complication with dysentery that is so common, which not only contributes materially toward the exhaustion of the patient, but also apparently prevents the

[1] Gaz. des Hôp. 1859. Nr. 20.

abscesses from opening so often externally as is the result when this disorder is not coexistent. According to the observations collected by Rouis, out of 24 abscesses not attended by dysentery, 19 (*i. e.*, more than two-thirds) discharged their contents externally; out of 118, on the other hand, accompanied by dysentery, only 58 (*i. e.*, one-half); of the former, 14 recovered (*i. e.*, about three-fifths); of the latter, 25 (*i. e.*, somewhat more than one-fifth).

In the temperate zone the fatal termination of the disease is not less frequent than in the tropics. The statement of Frerichs —not in accord with the above—would apply, at most, as he himself moreover intimates, to traumatic hepatitis; as regards this variety, however, no more favorable rate of mortality is obtained from the statistical data to be found in the literature of the past thirty years than that above quoted with respect to uncomplicated tropical hepatitis; of the twelve cases, seven terminated in recovery, three as the result of operation and four after perforation, the abscesses bursting respectively into the stomach, intestine, pelvis of the kidney, and bronchi. It would seem highly probable, therefore, that a larger proportion of the cases terminating in death than in recovery remain unpublished. When the cause of the malady could not be determined, only a small number of cases were cured, apart from those of traumatic origin, while in some of the recorded observations included under this category, it is, moreover, doubtful whether the case was not one of suppurating echinococci.[1] When the formation of pus in the liver has been preceded by some affection of the bile-ducts, or where it is of metastatic or pyæmic origin, the termination in death constitutes the rule to such an extent that in the list of cases to which reference has been made I have found but a single observation—omitting an accidental co-existence of external injuries with hepatitis—which might be regarded

[1] The great majority of observations respecting hepatic abscess terminating in recovery, contained in the French and English literature, relate to individuals who have been sooner or later taken ill after returning from a temporary residence in a hot climate, the symptoms simulating those induced by a fully-formed hepatic abscess; it is hardly necessary to remark that such cases should not be embraced in the statistics of hepatitis of the temperate zone.

as an exception. This relates to the following case reported by Vedrènes:[1] Robust man, twenty-four years old; wound from a sword-stroke on the right parietal bone, and on one hand; after the twenty-first day extensive suppuration of the wounds; after the twenty-third day repeated chills; subsequently pain in the hepatic region, especially in the vicinity of the left lobe; gradual formation of a tumor between the ensiform cartilage and the navel; perceptible fluctuation; opening of the abscess after the previous application of caustic; discharge of half a tumblerful of pus; after prolonged suppuration, complete recovery.

The fatal termination is most frequently consecutive upon exhaustion from long-continued suppuration, fever, derangement of the digestion, etc. It often happens that the processes (pyæmia, affections of the bile-ducts, ulcerations of the large intestine) giving rise to or complicating the hepatitis, contribute very materially to the exhaustion, and under certain circumstances even more than the hepatitis itself. A similar effect is produced by the consecutive pleurisy, especially the purulent form produced by perforation.

Death may be brought on at a more rapid rate; with relative frequency by diffuse peritonitis, where it may be produced by propagation of the inflammation from the serous capsule of the liver, or by the discharge of the contents of the abscess into the abdominal cavity; occasionally by pericarditis, either perforative or induced *per contiguitatem*, and by the formation of metastatic deposits in the lungs after thrombosis of the hepatic veins; rarely by too great extension of the pneumonia caused by an advance of the suppuration into the lungs; in quite exceptional cases, by the abscess perforating into the *vena cava;* by hæmatemesis, or bronchorrhagia, where it bursts into the stomach (De Castro, loc. cit., p. 19) and bronchi (Bitchey) respectively.

In endemic hepatitis, according to the statement of observers, *recovery* may take place in the first stage, before the commencement of suppuration. At many times (*En temps d'endémie bénigne:* Dutroulau, loc. cit., p. 626) such cases constitute the greater number. As a rule, their duration is from one to two

[1] Rec. de mém. de méd. mil. 1869, Avr., p. 329.

weeks, though they not unfrequently leave behind a long-continued enfeebled condition of the patient, an enlargement of the liver, subsiding only quite gradually, and a tendency to relapse.

Where the formation of an abscess has already begun, recovery does not usually follow until the pus has been discharged externally. Passing over, at this point, those cases of recovery brought on by aid of operative interference, there will be found three principal channels by which the evacuation may occur: by way of the bronchi, the digestive canal, and the external parietes; the first mentioned being that by means of which the road is most frequently (absolutely and relatively) paved for a favorable termination; the second being considerably behind the first as regards absolute frequency, though but slightly so as regards relative frequency. According to the statistical data of Rouis, out of 30 patients, in whom the abscess opened into the air-passages, 15 recovered; out of 14, where the pus discharged into the stomach or intestine, 7. According to De Castro, out of 25 cases of the first class there occurred 19 recoveries, and out of 17 of the latter class, 11 recoveries. According to Heinemann, the evacuation through the lungs is the mode most favorable to recovery. Dutroulau (loc. cit., p. 631) considers the bursting into the digestive canal more favorable, without, however, fortifying this theory by figures. The opening of the abscess through the abdominal or thoracic wall, when left to itself and not expedited by artificial aid, leads but seldom to recovery; this is attributable partly to the fact that, on account of the length of time commonly required for the abscess to discharge its contents externally, when this course is taken, it usually attains a considerable magnitude; partly, however, to the circumstance that the operation is usually omitted only in those cases in which, owing to the enfeeblement of the patient, no benefit can be thereby expected. Where perforation takes place into the pelvis of the kidneys, recovery may follow, as is proved by the observation of Huet, above referred to, and by two other instances discovered by him in the literature of the subject. The length of time from the beginning of the discharge of the pus to the completion of convalescence will vary, of course, according to the circumstances of the individual case, and may be prolonged to such an extent,

especially by complications (dysentery, malarial diseases) or consecutive disorders of digestion, that it is extended over several years. As a rule, it amounts to only from one to two months, and instances of still more rapid progress in recovery occur in all three modes of evacuation. After perforation into the bronchi one of Rouis's patients recovered in seventeen days; of De Castro's one recovered in seventeen days, one in fifteen, and one in twelve; the patient in the clinique of Th. Weber, whose history is reported by Tophoff, was discharged *cured* nineteen days after perforation into the stomach; in the single case in which Rouis (loc. cit., p. 160) saw recovery ensue after spontaneous bursting through the external wall, this followed within fifteen days.

In many cases the result is but an *incomplete healing* of the abscess: if its walls are too callous to admit of sufficient approximation, then the secretion of pus continues, though possibly in diminished quantity, and prevents the closure of the passage leading outward; a permanent fistula is thus formed between the cavity of the abscess reduced in size and the external covering, or the bronchi. According to two observations by Petit Fils, cited by De Castro (loc. cit., p. 38), the communication with the intestine may remain open for a period of years. Martenet saw a soldier in Algiers who was obliged to have an hepatic abscess punctured every two or three months, in the meanwhile attending to his duty; upon each occasion a glassful of thick pus was discharged, and in two or three days the opening had again closed; within a period of scarcely four years puncture was here performed twenty-four times.

It can be safely asserted that small hepatic abscesses, which have not previously discharged their contents, may undergo cicatrization after the reabsorption of the serum and pus-cells that have sustained molecular disintegration; for such cicatrices, similar to those left behind by healed abscesses after the evacuation of their contents, have been found in the liver, either alone or accompanied by purulent deposits, by several observers[1] on

[1] Compare *Cambay*, loc. cit., p. 223; *Haspel*, loc. cit., pp. 239 and 240; *Morehead*, loc. cit., p. 346; *Dutroulau*, loc. cit., p. 346; and the observations of *Budd* and *Greenhow*, above cited (p. 130).

post-mortem examination of individuals who had exhibited during life unequivocal symptoms of hepatitis. A case reported by Cas. Broussais shows that even several abscesses contained in a liver may all become cured in the manner above indicated; in a man, thirty years of age, who had been discharged as convalescent after an attack of dysentery and hepatitis, but who, after a recurrence of the former affection, had died, there were found seated on the convex surface of the liver four white, radiating, hard cicatrices, though the organ did not present any other inflammatory alterations.

That recovery is possible, however, even where several large abscesses exist, provided these all open externally, appears to be demonstrated by a case observed by Goodwin,[1] which, being unique, is here given in abstract:

In a woman, aged thirty-eight years, after the reception of a blow in the region of the liver, there arose violent pain at that part, fever, with delirium and considerable swelling of the right side; during a severe attack of choking there was suddenly vomited over one-half pint of offensive pus, which continued to be discharged in this manner in diminished quantity daily for the next three weeks, the right side being, meanwhile, reduced in volume. Three and one-half months after the wound, recurrence of severe symptoms of hepatitis: the right hypochondrium projecting considerably and tense; the lower margin of the liver perceptible upon palpation from the right iliacal region to the navel. Fourteen days later there followed spontaneous rupture between the ensiform cartilage and the navel immediately to the right of the median line, with the evacuation of one-half pint of foul-smelling pus; five days later, opening of a second purulent collection beneath the middle of the right inferior margin of the ribs; and again, nine days later, opening of a third abscess at a point between the first two, with a discharge each time of about a pint of offensive pus. At the expiration of about two months the two openings last formed closed, whereas the first was still secreting at times brownish serum, at other times thick pus. By the tenth month after the illness the patient was convalescent, but the discharge from the fistula still continued.

Suppurative hepatitis is an extremely dangerous disease. The *prognosis* may be here rendered still more unfavorable by complications with dysentery, obstinate intermittent fever, and, in general, with those processes which accelerate exhaustion; it is almost absolutely unfavorable when the affection is of pyæmic origin, or when it is attributable to some lesion of the bile-

[1] Brit. Med. Jour., Sept., 1864.

ducts, and likewise when exudative pleuritis, metastatic disease of the lungs, or extensive pneumonia supervenes. If diffused peritonitis or the pericarditis of perforation is induced, death is then close at hand. The cure of hepatic abscesses which have not discharged their contents is of such extremely rare occurrence, that when the diagnosis is certain, the possibility of such a result is hardly to be taken into consideration. When the abscesses open externally, it is of little importance, in a prognostic sense, through which organ this rupture takes place; but it is a matter of material consequence whether or not, consecutive upon this opening, the symptoms of the disease abate, and completely disappear; for the persistence or recurrence of febrile appearances must awaken apprehension that the ruptured abscess is of too long standing to become cicatrized, or that there may be concealed in the liver still other inflammatory deposits. Dutroulau warns against giving an absolutely favorable prognosis even after an operation has resulted in the healing of the abscesses.

Treatment.

We will consider first the treatment of the disease in the stage preceding suppuration, which, as has been already stated, comes but very rarely under observation in our climate, except in traumatic cases.

In cases of recent origin, acute hepatitis calls for antiphlogistic remedies. *Venesection*, which was formerly regarded almost universally as the most powerful antiphlogistic in this disease, is recommended—in copious application—even up to the most recent times by French and English physicians. Frerichs, who mentions the objections brought forward by van Swieten to this plan of treatment, and points out its, to say the least, doubtful utility, regards it as indicated only in robust individuals where there is great hyperæmic swelling and tenderness of the liver and urgent dyspnœa. But even under such circumstances its application seems in our day no longer justifiable. In the present state of our knowledge, we cannot ascribe to venesection any direct influence upon the inflammatory processes, and its antifebrile effect is very transitory. To the latter influence is in all

probability to be referred the fact that immediately after blood-letting the respiration is wont to be easier. But the principal cause of the dyspnœa is the sensitiveness of the acutely swollen liver; and for the reduction of this symptom there are remedies which fulfil this indication in a direct manner, and with far less danger to the general strength of the patient.

Among the remedies of this class, *local abstractions of blood* and purgatives have from ancient times occupied an important position in the treatment of acute hepatitis. Phlebotomy is practised with greatest advantage[1] by the application of a number (10–15) of leeches in the immediate vicinity of the anus, the cutaneous veins of this region being in communication with the roots of the portal vein; or leeches and also cupping-glasses may be applied in the region of the liver, provided this organ is very sensitive to external pressure, which is particularly liable to occur in traumatic hepatitis resulting from early implication of the serosa. In such cases advantage will also be derived from the local application in the form of cold compresses frequently (every five minutes) changed, or from ice-bags moderately filled.

For *purgatives* many prefer to employ large doses of calomel. This is administered daily by Rouis for several consecutive days in gramme doses, either at one time or divided into three or four portions; and this he recommends rather than the less energetic agents, such as castor-oil, Glauber's salts, and citrate of magnesia, when it is desired to arrest the progress of prodromic hyperæmia. According to the experience of others, where decided inflammation exists the milder vegetable and saline purgatives are efficacious, or they at least suffice to keep up the increased action of the bowels when once excited by a few doses of calomel. In order to establish this action, however, it may even be requisite in very severe cases to combine a drastic cathartic with the calo-

[1] *Maclean* (The Lancet, July 12, 1873, Jahresbericht von Virchow und Hirsch, 1873, II., S. 167) and *Berenger-Feraud* have recently recommended the direct abstraction of blood from the liver by means of the aspirator of *Dieulafoy*, to effect which a puncture should be made with the trocar to a depth of 5–15 centimetres. According to *Maclean*, the most striking abatement of all symptoms is thereby produced; and *Berenger-Feraud* saw recovery in two cases of acute hepatitis where he had withdrawn blood (100 grammes at a time) in the manner indicated (*vide* p. 161).

mel. Purgatives are considered to be contraindicated where there is great sensitiveness of the epigastrium or frequent vomiting; their employment should not be resorted to until the irritation of the mucous lining of the stomach has been allayed by the application of leeches to the epigastrium and by narcotics.

Under the remedies employed with the object of attempting to reduce the engorgement of the liver, should be included also *emetics*. These agents are recommended also by Rouis for the relief of violent well-marked "bilious symptoms." They manifestly promote the discharge of the blood and bile from the liver, because during the act of vomiting a compression is produced on all sides of the organ. Their employment should be restricted, however, to the early stages of the disease, while there is reason to believe that inflammatory deposits are not yet present; and even then they are of doubtful utility. Annesley observed a brief improvement under their use, followed by a proportionately severe aggravation of the symptoms.

The exhibition of small doses of calomel pushed to the point of salivation has been long employed, especially by English, and, with far less frequency, by French physicians, as a remedial measure which was thought to exert a direct influence upon the inflammatory process. Of late this procedure appears to be but seldom resorted to, and surely with good reasons. For, even if the objection urged by Budd against this medication—that the development of the abscess may begin before the mercury can produce any decided constitutional effect—is not altogether correct, still proof is as yet wanting, with respect to hepatitis as well as the acute inflammation of other organs, that the disease can be arrested in its course by mercurial treatment. In case of hepatitis this is decidedly improbable; for trustworthy authors (Twining, for instance) have observed the transition into the stage of suppuration in patients in whom salivation had already appeared; while in those cases, upon the other hand, where the employment of mercury was followed by resolution, some other antiphlogistic measures had invariably been resorted to. When confronted, then, by a disease which in its subsequent course gives rise so frequently to exhaustion, there are sufficient grounds for abstaining from a procedure which is calculated, even from

the outset, to materially impair the physical power of resistance. Inunction with gray ointment in the vicinity of the affected organ seems more admissible, when not employed in such quantity as to likewise excite thereby a general hydrargyrosis. Where this effect is, however, not produced, it remains at least quite incomprehensible how any action of the medicament can be communicated from the abdominal parietes to the liver.

Objections, similar to those raised against the mercurial course, are applicable to the treatment by means of tartarized antimony formulated according to the method of Rasori, which, combined with local abstractions of blood, has been highly recommended as a very efficient antiphlogistic by several French physicians resident in St. Louis, whose observations have been reported by Dutroulau (loc. cit., p. 637). The reduction of the fever, which is probably the only favorable result that can take place under this treatment, can be effected with greater certainty by means of quinine or digitalis. The use of the latter for this purpose has been advised by Rouis, though, in view of the experience derived from other diseases, the doses prescribed by him—one grain and a half (one decigramme) every six to eight hours—appear much too small.

As regards hydrochlorate of ammonia, spoken of in commendatory terms several years ago by W. Stewart,[1] an English army surgeon, who administered it after previous blood-lettings, in doses of 18 grains (1.2 grammes), morning and evening, as long as indications of hepatitis are present, further observations are wanting.

Vesicants have been resorted to by some, even at the height of the disease; though by the greater number not until the more violent symptoms have yielded. De Castro attributes to them a decided influence in reducing the pain and tumefaction of the liver; Haspel[2] observed dense inflammatory deposits diminish and gradually disappear under their use.

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[1] The Lancet, 1871. I., 19, 21.

[2] *Sachs*, too, extols the value of a large blister, especially in those cases where, at the very commencement, the sensitiveness upon palpation is remarkably great, and advises that the derivation be kept up for several days by means of plasters spread with irritating ointment.

After the fever has subsided, warm wet compresses and warm baths are calculated to hasten the resorption.

For pain and sleeplessness the preparations of opium, given internally or subcutaneously, may become requisite as palliative agents.

In complications with dysentery, copious blood-letting, emetics, and purgatives are contraindicated.

In acute hepatitis the diet should be restricted to easily digested, liquid nutriment, thin soups, diluted milk, and acid drinks; alcoholic liquors are to be absolutely avoided. Convalescents should return very gradually to solid articles of food.

When the symptoms of hepatitis are developed in a less acute manner, the treatment will then be proportionately simplified. In such cases blood-letting is usually unnecessary. The application of an emetic, upon the other hand, according to the observations of Rouis, tends often to favor a shorter duration of the prodromic hyperæmia. Subsequently milder laxatives, narcotics, and vesicants are generally sufficient.

If the affection is inclined to run a slow course, its treatment will not differ essentially from that of chronic hyperæmia of the liver. The principal indication then is to prescribe a diet appropriate for sustaining the strength of the patient, eschewing everything that would tend to produce an irritative effect upon the digestive organs or the liver, and providing, in the meanwhile, by means of the mildest agents, for the frequent evacuation of the bowels. Treatment with simple water is often admissible, or, still better, waters containing the muriate of soda, such as Vichy and Ems. These are probably the cases for which Heinemann believes the use of the Carlsbad waters may be confidently recommended with the view of preventing the formation of abscesses. The best remedy for Europeans resident in the tropics is, as a rule—though not invariably—a return to a temperate climate.

When, notwithstanding the treatment directed toward the inflammation, indications of suppuration set in, all interference having a weakening tendency must be avoided. For the relief of the inflammatory symptoms perchance still continuing, or recrudescent at a later stage, it is better to restrict ourselves to the application of cutaneous irritants (moist, warm cataplasms,

vesicants) in the region of the liver, and laxatives. Mercurials, according to the unanimous opinion of all good observers, are positively injurious after the commencement of suppuration. It is of the greatest importance to prevent, as far as possible, the exhaustion that threatens, sooner or later, in this stage. The patient should be nourished as well as the condition of the digestive organs will permit. Spirituous drinks, such as beer and wine, are also now admissible. Among the cases reported by English physicians are many terminating favorably in which even brandy was liberally given. Preparations of quinine and—provided fever is not present—the chalybeates are also appropriate on account of their tonic effect. *Aqua regia*, recommended first in India and subsequently in England, is, at most, of very questionable efficacy.

Particular symptoms indicate special remedies. If the bowels are inactive, it is well to prescribe rhubarb, aloes, senna, and like agents, in doses which will excite mild cathartic action. Diarrhœa should be combated by means of vegetable and mineral astringents and opium. Sleeplessness and pain require the administration of narcotics. Antipyretic medicaments prove, almost without exception, powerless against the fever in its various forms; it is, therefore, no doubt better either to refrain entirely from their use, or else to abandon them as soon as they prove inefficient, because disorders of the stomach or intestines may easily be produced by their prolonged administration.[1] The attempt to allay the fever by cooling baths is—independently of the fact that it would be, in all probability, quite as useless as in case of suppurative fever—inadvisable, for the reason, viz., that the unavoidable movements of the patient thereby made might favor the rupture of the abscess into the abdominal cavity. This possibility requires consideration even in those cases where we can diagnosticate with certainty an abscess so situated as not to give rise to any such apprehensions; for we can never be sure

[1] According to my experience respecting the antipyretic action of salicylate of soda, in doses of 4.0 to 6.0 grammes, which, at least, is quite as sure in its action as the correspondingly larger doses of quinine, I should assign the preference to this agent for counteracting the fever in suppurative hepatitis, because it appears to exert far less frequently than quinine an unfavorable influence upon the digestive organs.

that, in addition to this abscess, still another less favorably located may not be present. On this account it seems that we should let the patient maintain constantly as quiet a posture as possible, if not strictly the continuous recumbent posture, as is insisted upon by Ward.

The treatment can be directed toward the abscess itself only when this admits of artificial opening. That this procedure is, under certain circumstances, admissible, admits of no doubt. The objections raised thereto will appear, when closely examined, unsound. Thus Budd fears the entrance of air into the wound, whereby a new inflammation may be excited, and gangrene with rapidly fatal termination induced. It need hardly be remarked, however, that this accident is also possible after spontaneous opening, although, as is shown by experience, it is of very rare occurrence. If, moreover, we have been warned against this operation, because danger is incurred of puncturing a distended gall-bladder or a cancerous nodule instead of an hepatic abscess, this caution bears upon the weak side of the diagnosis rather than of the therapeutic treatment. Finally, the operation has been condemned by some physicians (Jos. Franz, J. Martin, Maclean), as offering too few favorable results. This conclusion is, at the most, admissible only as regards the observations of former times, where want of success is to be ascribed chiefly to the faulty mode of operation, in so far as sufficient precautions were not taken to absolutely prevent the entrance of pus into the abdominal cavity.

The conditions which favor artificial opening are indicated by the following considerations. With extremely rare exceptions hepatic abscesses become healed only when they have discharged their contents externally; every procedure, therefore, which tends to accelerate this evacuation, must *ceteris paribus* be conducive to a cure. But the local as well as the general conditions present at that juncture, when the artificial opening begins to be possible, are almost invariably more favorable than subsequently, when the rupture occurs spontaneously. For an abscess closes up the more readily when it is recent and of small extent; and the physical strength of the patient falls off more and more with the prolonged continuance of suppuration. It results, therefore,

that the danger of the formation of secondary abscesses or of perforation into a serous cavity is much greater before than after the opening. Hence it is obvious that the sooner the artificial opening is resorted to the greater will be the chances of a favorable termination; or, in other words, the operation is indicated at the earliest moment practicable.

This leads to the question, Under what circumstances is the abscess fit for operation? Until recently the opinion prevailed almost universally that we should have recourse to operation only when the point upon the abdominal or thoracic wall beneath which the abscess is located is accurately known, and when at the same time the presence of adhesions between the visceral and parietal serous membranes in its vicinity has been definitely determined. Where there exists either a perceptible fluctuation, a phlegmon of the external parietes, or a painful prominence of the soft parts attended with œdema in the region of the false ribs, there remains then no doubt that the suppuration has already either extended to the abdominal wall, or has succeeded in penetrating the diaphragm. But, under these circumstances, also, the abscess has usually already attained a considerable size. The opening may be made by means of a bistoury, or an ordinary trocar. If, on the other hand, only an œdema or obscure deep-seated fluctuation can be detected at the seat of the circumscribed swelling upon the abdominal wall, we cannot calculate with certainty upon the existence of adhesions; this can only be assumed when the projecting part does not change its position upon the abdominal wall with the movements of the diaphragm, or with the most varied postures of the body.[1] If this condition is not present, or if there remains any doubt in this particular, in order to produce, next, an adhesive inflammation of the peritoneum in the vicinity of the abscess, an incision may be made in the abdominal wall, extending either to the parietal peritoneum (Graves[2]), or to the liver (Bégin[3]), and the wound dressed with

[1] *H. Cooper* (loc. cit.) considers it a sure indication of adhesions in case of uncertain fluctuation, if the base of the prominence is entirely surrounded by an indurated margin sensitive upon pressure, and recommends then that the opening be resorted to without further delay.

[2] Dublin Hospital Reports. May, 1827. [3] Jour. hebdom. 1830. I., p. 417.

charpie; or the abdominal wall may be gradually perforated by means of caustic potash (Récamier[1]). The last-mentioned procedure, being regarded as the most certain, is usually resorted to, but it is also the most painful, and—what is of still greater importance as regards persons in a failing condition—the most tedious. Moreover, it is inapplicable to the thoracic wall, because of its tendency to produce caries of the ribs. In making an incision extending to the liver, the danger arises, as has been observed by Haspel and Rouis, that the liver may not force its way into the wound, and consequently no adhesion between this organ and the abdominal wall is effected.

Many English and French surgeons (H. Cooper, R. Martin, Cameron, De Castro, P. Garnier, and others) have of late preferred puncture to all other methods, allowing the canula to remain. This procedure consists in plunging a trocar of average size[2] into the abscess, and allowing the canula to remain until it begins to rest loosely in the enlarged artificial canal, which usually occurs upon the third day. The instrument is then removed, and its place supplied either (R. Martin) by a small piece of linen saturated with oil, or (De Castro) by a drainage-tube, which should be changed as often as necessary and removed altogether whenever the small quantity of the discharge and the general condition of the patient justify the conclusion that the abscess is about healed. By this means an adhesion[3] between the liver and abdominal wall, if not already present previous to the puncture, can be effected with greater certainty than by the method of Récamier, for the inflammatory irritation is here excited not merely—as when the abdominal parietes are perforated by means of caustic—in the parietal fold of the peritoneum, but also directly in the serous capsule of the liver. Moreover, the irritation induced by the wound from a smooth canule is, at

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[1] *Velpeau*, Méd. opérat. 2. éd. IV., p. 19.

[2] *De Castro* uses a trocar the stilette of which is hollow and provided with lateral openings, corresponding to which are found openings in the wall of the canula. In consequence of this arrangement, as soon as the abscess is reached, pus flows at once from the handle of the instrument.

[3] *Murray* (loc. cit.), as early as in 1842, called attention to the advantage of puncture, in that it promotes adhesions between the liver and abdominal wall.

all events, less severe than that excited by caustic potash, or by charpie packed in an incised wound of the peritoneum ; while the danger of diffused peritonitis is less in case of puncture than in the other methods. That the irritation of the canule is sufficient to produce this effect is demonstrated by an observation of Jameson,[1] who found, in a case terminating fatally upon the fourth day after the puncture, adhesion of the liver with the abdominal wall around the artificial opening for a breadth of 1½ ctms. The method in question presents also, in addition to the above advantages, the following : it gives rise to very little pain ; it is not, like incision, attended with the loss of blood ; it does not, like cauterization, produce a loss of substance in the abdominal parietes ; it produces most promptly the desired effect ; it is applicable in every case where an abscess can be diagnosticated at a point at all accessible to the trocar.[2] The latter circumstance renders this method especially valuable in endemic hepatitis, where, from causes previously stated, the nature of the disorder can be often recognized even at an early stage : here a slight prominence or a great sensitiveness at a circumscribed point of the enlarged liver points to the seat of the purulent deposit, and it is not necessary to postpone the operation until œdema or fluctuation has appeared. Some go still further, considering puncture admissible when, indeed, the diagnosis of abscess-formation is certain, but when the location of the abscess is altogether unknown. Thus, De Castro says (9 loc. cit., p. 5) : "Quand je ne connais pas le point où se trouve l'abcès, je ponctionne au milieu des limites du foie, au centre de son plus grand diamètre vertical ;" and cites numerous cases where the operation was undertaken by himself and other physicians in Alexandria once, twice, and even three times, without finding pus. In none of these cases was the interference attended

[1] The Lancet. April 29, 1871.

[2] *Sachs* suggests still another very considerable advantage, that by the application of the trocar a gradual and intermittent discharge of the abscess may be effected, by which means the neighboring parts may after a while become approximated, and the cavity compressed. In this way we avoid, as far as possible, the bursting of the blood- and bile-vessels running through the walls of the abscess, and the extremely dangerous ruptures of the adhesions connecting the liver with the neighboring parts.

by any bad results. In one instance, after the evacuation of several ounces of blood from the opening made by the puncture, there was experienced a remarkable diminution in the volume of the liver, and an improvement in the condition of the patient. According to the statement of R. Martin, English physicians in India followed precisely this course, and observed thereafter very favorable results, the symptoms of the disease disappearing very soon after the operation. Although it is more than probable that the observations last quoted did not relate to cases of suppurative hepatitis, but to those of simple or inflammatory hyperæmia of the liver, and although, in the treatment of hepatic abscess, such an operation in the dark surely does not deserve to be imitated, the experiments are, nevertheless, of interest, as affording proof that puncture of the liver is, as a rule, quite free from danger, and that it does not involve the risk of a hemorrhage or new inflammation, as has been alleged by Budd. This fact is illustrated also by the experiments performed by De Castro, Lavigerie, and others upon animals (rabbits, cats, dogs), from which it results that puncture of the liver by means of an explorative, or even a hydrocele trocar, does not give rise to either the least acute inflammatory attack or other disturbances, and, as was demonstrated by the autopsy subsequently made, leaves behind no mark whatever, or, at the most, a punctiform cicatrix in the hepatic capsule. The harmlessness of wounds inflicted by very fine instruments is illustrated by the result of the experiments instituted by Trousseau, with the object of producing adhesions between abdomen and liver in echinococcus of the latter organ. This experiment consists in multiple acupuncture, the needles being left remaining for several hours. This procedure is not applicable, however, in hepatic abscesses, because the mechanical irritation is operative for too short a time to produce firm adhesion between the two surfaces of the peritoneum; and, when the needle has opened the purulent deposit —which cannot with certainty be avoided—after its removal, a purulent inflammation of the serous envelope of the liver may be readily excited by this accumulation forcing its way into the wound in this membrane.

As regards the further treatment of abscesses that have been

artificially opened, the reader is referred to the handbooks of surgery. It may be remarked here, however, that in many instances, by means of suction with the aid of the syringe or (De Castro) cupping-glasses, applied several times daily to the orifice of the puncture, the discharge of the pus has been effected, without giving rise thereby to severe hemorrhage or other collateral unfavorable result. McConnell,[1] of India, has applied Dieulafoy's pneumatic aspirator with results comparatively quite favorable, especially in smaller abscesses; in large ones, free drainage is, according to this author, the most appropriate.[2] Where the cavities are extensive, or where their contents possess a fetid character, it has been found of service to syringe them out with water, and likewise with solutions of iodine, creosote, or carbolic acid. It is hardly necessary to warn the physician that the patient must guard against straining movements, in order not to incur the danger of rupturing the adhesions, which, as happened in a case quoted by Rouis, may result in sudden death.

As regards the results of operative opening, the reports vary quite materially: Curtis (1782) observed but two recoveries among ten persons operated upon; J. Clark had eight recoveries among thirteen cases; Murray obtained a favorable result six times in seventeen cases; according to the statistics collected by Waring, in eighty-one operations there occurred but fifteen recoveries (*i. e.*, less than one-fifth); of sixty-one cases collected by De Castro, thirty-four terminated in recovery.

In the literature of the last fifteen years accessible to me I have found, besides the cases of McConnell previously mentioned, detailed reports of thirty-four operations. Of these twenty-two terminated in recovery. In the greater number of cases ending fatally the operation was not resorted to until late (after fluctuation had already appeared). Among those recovering there are,

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[1] Of fourteen patients, who were between twenty-four and forty-five years old, and all reduced in the highest degree, six died; eight recovered. The puncture had to be repeated in most cases—in one instance as many as eight times in all; but in several patients a single puncture was sufficient.

[2] *Sachs* recommends, in large hepatic abscesses, the double puncture suggested by *Simon* as a method of operating upon echinococcus cysts.

nevertheless, found also several with respect to whom the quantity of pus that poured out immediately after the puncture (in Pacheco's[1] case five pounds, in that of R. Bennet[2] as much as six pints) justified the conclusion that the abscess was of very considerable size. Where the abscess contained but a few ounces, the patients recovered rapidly, not unfrequently even in three weeks; in the traumatic case of Fischer, already previously referred to, where from eight to ten ounces were evacuated by means of an incision, recovery ensued in the same length of time; so, likewise, in the traumatic case reported by Borius, where the cavity contained 200 cubic centimetres, recovery was complete in five weeks after the incision. In no instance could any connection be traced between death and the operation, which, on the contrary, was almost invariably followed shortly after by an amelioration of the morbid symptoms; the autopsy revealed the presence either of still other abscesses in the liver in addition to the one artificially opened, or of consecutive pleuritis, pericarditis, etc., but never diffuse peritonitis.

When the abscess has spontaneously broken through the external integument, then the extensive ulceration of the abdominal or thoracic wall requires at times especial attention as regards treatment.

To relieve the chronic hepatic fistula remaining behind after spontaneous or artificial opening, Rouis, who ascribes the cause of this lesion to an inflammatory enlargement of the liver (un fond d'engouement au sein du foie), recommends the internal and external use of sulphurous mineral waters as the only efficacious remedy. In one case, where the fistula had already existed more than six months, Lanchlan Aitken[3] observed rapid recovery take place after pure iodine had been injected three times.

Where perforation into the lungs occurs, the local application of cold and the administration of irritant expectorants or antiseptic inhalations may be necessary. After perforation into

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[1] Gaz. méd. de l'Algérie. 1871. Nr. 7. Virchow und Hirsch's Jahresber. f. 1871. H. 1, S. 160.

[2] The Lancet. 1860. I., 7.

[3] Edin. Med. Jour. June, 1870.

the pleura, if the strength of the patient is not already too far reduced, the operation for empyema is indicated, which, when undertaken as early as possible, may possibly lead, upon the whole, more frequently to a favorable result than would be expected in view of previous experience. Where the pus empties into the abdominal cavity, the attempt should be made, by means of absolute rest and large doses of opium frequently administered, to counteract the spread of the peritonitis, which, in a case observed by Stokes (l. c., p. 111), appears, by way of exception, to have been accomplished. After the abscess has opened into the digestive canal or the kidneys, no especial treatment is, as a rule, required.

Interstitial Inflammation of the Liver. Hepatitis Fibrosa. Cirrhosis of the Liver.

I. Usual or Genuine Form of Cirrhosis, Cirrhosis of Laënnec; Granular Induration or Granular Atrophy of the Liver; Granular Liver.

Laënnec, Traité de l'auscult. médiate. 4. éd., T. 2, p. 501.—*Boulland*, Mém. de la Soc. d'émulat. T. 9, p. 170.—*Andral*, Clin. médic. T. 4, p. 198-213 (4. éd., T. 2, p. 243).—*Bright*, Rep. of Medical Cases. 1827, p. 89-110. Plates 6 and 6* of Guy's Hosp. Reports. Vol. I. 1836.—*Kiernan*, Philosoph. Transact. 1833. —*Cruveilhier*, Anat. patholog. Livr. 12, Pl. 1.—*Carswell*, Illustrations of the Elementary Form of Diseases. Lond., 1838. Fasc. 10, Pl. 2.—*Hallmann*, *Ed.*, De cirrhosi hep. Diss.-Inaug. Berol., 1839.—*Becquerel*, *Alfr.*, Arch. génér. Avr. et Mai, 1840.—*Schuh*, Zeitschr. d. Wien. Aerzte. Bd. 2, S. 360.—*Oppolzer*, Prager Vierteljahrschr. Bd. 3, S. 17.—*Henle*, Zeitschr. f. ration. Med. Bd. 2, S. 253.—*Budd*, Krankh. d. Leber, deutsch v. Henoch. S. 125-159.—*Wunderlich*, Hdb. der Pathol. u. Ther. 2. Aufl., Bd. 3, S. 313.—*Bamberger*, Wien. medic. Wochenschr. 1851. Nr. 1, 4, 9, 11.—*Monneret*, Arch. génér. Août et Sept., 1852.—*Gubler*, De la cirrhose. Paris, 1853.—*Koller*, De hep. cirrhosi. Diss. Berol., 1854.—*Cohn*, Guensburg's Zeitschr. Bd. 6, Heft 6.—*Bamberger*, Krankheiten des chylopoet. Syst. 2. Aufl., S. 510-527.—*Klinger*, Virch. Arch. Bd. 12, S. 549.—*Redenbacher*, *Hg.*, Ueb. d. Zusammensetzung hydropischer Transsudate bei Lebercirrh. Inaug.-Diss. Augsburg, 1858.—*Wallmann*, *H.*, Oesterr. Ztschr. f. prakt. Heilk. Bd. 5, Nr. 9.—*Tuengel*, Klin. Mittheilungen a. d. J. 1858. S. 127, a. d. J. 1859. S. 163.—*Sappey*, Bull. de l'Acad. de Méd. T. 24, p. 943.—*Frerichs*, Klinik der Leberkrankh. Bd. 2, S. 19-90.—*Henoch*, Klinik der Unterleibskh. 3. Aufl., S. 84-90.—*E. Wagner*, Arch. d. Heilkunde. 3. Jahrg., S. 459.—*Liebermeister*, Beiträge z. pathol. Anat. u. Klinik d. Leberkh. S. 29-76.—*Botkin*, Virch. Arch. Bd. 30, S. 456.—*Foerster*, *Gst.*, Die Lebercirrhose nach pathol. anatom. Erfahr. Inaug.-Diss. Berl., 1868.—*Hauerwaas*, *Frz.*, Zur Casuistik d. Lebercirrh. im Kindesalter. Inaug.-Diss. Würzb., 1871.—*Habershon*, *S. O.*, Guy's Hosp. Rep. 3. Sér., Vol. 16, p. 389.—*Duchek*, Wiener medic. Presse. 1871. Nr. 49-51.—*Legg*, *J. Wickham*, St. Barthol. Hosp. Rep. Vol. 8, p. 74. Jahresber. von Virchow und Hirsch für 1872. Bd. 2, S. 164.—*Cornil*, Arch. de physiol. norm. et patholog. 1874, p. 264.—*Borelli*, *D.*, Verhdlgn. der physik. medic. Ges. in Würzburg. N. F. Bd. 8, S. 87.—*Leudet*, Clinique médic. de l'Hôtel-Dieu de Rouen. Paris, 1874, pp. 48-66, 540-549,

557–565.—*Charcot et Gombault*, Arch. de phys. norm. et pathol. 1876, p. 453. —*Charcot*, Leçons sur les mal. du foie. Progrès méd. 1876.—*Stricker*, Charité-Annalen. 1. Jahrg. 1876. S. 324.

Historical Account.

The knowledge of the disease under consideration reaches back at least as far as the fourth century before Christ. Cœlius Aurelianus[1] observes, in discussing the causes of ascites: "Erasistratus jecur inquit pati: in aperitionibus enim saxeum semper inveniri confirmat." It is quoted by Aretæus as a well-known fact that inflammation of the liver not terminating in suppuration is followed by induration (σκιῤῥος) of the organ. Vesalius[2] describes the granular induration in the following words: "Hepar totum candidum et multis tuberculis asperum, tota anterior jecoris pars et universa sinistra sedes instar lapidis indurata." Posth[3] even makes use of the term now ordinarily employed by us; he found in addition to the ascites, "substantiam hepatis interius totam granulosam, granis nimirum quantitate pisorum ubique apparentibus." Morgagni[4] is the first to allude to the compression of the smaller hepatic blood-vessels, and the disturbance thereby induced in the function of the gland and in the abdominal circulation. The disease was described by some under the name *obstructio hepatis*, *marasmus hepatis* (Bianchi); others designate it by the term "tubercles" (Baillie) or "nodules" (J. F. Meckel) of the liver. It was not until the present century that attempts were made to elucidate the modes of origin of the anatomical changes. Laënnec, who was led from the yellow color of the granulations to designate the affection cirrhosis (from κιῤῥος, yellow), regarded the granulations as new formations, by the development of which the normal structure of the liver is destroyed, in consequence of which the organ, in place of becoming enlarged, may be reduced in volume. Boulland opposed this theory, maintaining that the granulations consist of the secreting substance, which, as the result of morbid

[1] Morb. chron. Lib. III., Cap. VIII.

[2] Opera. T. II., p. 674.

[3] Vide *Morgagni*, De sed. et caus. morb. Epist. 38.

[4] Ibidem.

changes in the highly vascular connective tissue (primarily hyperæmia, subsequently obliteration of the vessels), becomes more prominent than usual, and ultimately undergoes disorganization. Andral regards the essential feature of the process to be an hypertrophy of the parenchyma of the liver (termed by him "white substance") and a simultaneous atrophy of the red, highly vascular substance embedded in the areolar framework. Cruveilhier, who lays stress upon the presence of thick fibrous tissue in the cirrhotic liver, considers it most probable that, besides the atrophy of the greater number of the acini, there exists an hypertrophy of the remainder. An accurate knowledge of the histological process involved in cirrhosis was first obtained by the investigations of Carswell and Hallman. According to these writers the lesion is attributable to an increase and induration of the interlobular connective tissue, in consequence of which the lobules are pressed together and constricted; and this will account for the diminution in size of the organ, the impairment of its secretory function, and the impediment to the circulation within it. The granulations are composed of those lobules that have as yet been subjected to but little or no compression. This theory is, in the main, generally accepted, even at the present day. The results of more recent researches, in conformity with which the theory has in certain particulars been modified and perfected, will be considered in their appropriate place in the following chapters.

Etiology.

Among the causes of the affection, the immoderate use of brandy is the one the longest known and the most accurately demonstrated; hence, the English apply to it the term "gin-drinkers' liver." In Germany more than a third part of the cases are to be traced to this pernicious habit. Next after the *primæ viæ* the liver is obviously most liable to be rendered diseased by the action of alcohol; for this liquid, after its passage into the blood, is presented to it in a much less diluted form than to any other organ. The reason that not a few brandy-drinkers continue exempt from the disease is attributable per-

haps, in part, to the circumstance that after a certain amount of experience the indulgence in this habit has a less injurious effect, if at the same time food is regularly taken: the alcohol then reaches the liver at a slower rate and in more diluted form. For the same reason the disease is much less frequently induced by the abuse of beverages containing a less amount of alcohol. There admits of no question, however, that the prolonged excessive use of wine or strong beer can produce this effect. Numerous instances are found in the literature of the subject occurring in wine-drinkers as well as in beer-brewers, who strenuously denied that they ever indulged in brandy (Bamberger, Liebermeister, Leudet).

It has not been shown, with regard to any one of the other articles composing our food and drink, that they exert any influence in the production of cirrhosis; though Budd is inclined to ascribe such an effect to the irritant spices made use of in India.

The question as to the origin of the disease in the numerous cases where there has been no abuse of spirituous liquors, found first of all partial solution in the observations gradually accumulating, in view of which it was rendered more and more certain that two infectious diseases may give rise to the development of cirrhosis, namely, syphilis and intermittent fever. Dufour[1] had described, as early as in 1851, a case of cirrhosis of the liver associated with *syphilis;* and Virchow, in his article, "Ueber die Natur der constitutionell syphilitischen Affectionen,"[2] distinctly affirms that there is found at times in syphilitic livers an extensive induration, the result of development of the interstitial connective tissue, which may give rise to forms of cirrhosis. Next Frerichs—supported by the fact that of thirty-six cirrhotic patients coming under his observation, six were suffering from syphilis, or had formerly presented the symptoms of this affection—assigned at once to this chronic infectious disease a place in the etiology of cirrhosis. It must, indeed, be admitted that, in the cases belonging to this category, the process is not always developed with the same regularity throughout the entire organ

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[1] Bull. de la Soc. anat. de Paris. 1851, p. 139.

[2] Virchow's Arch. Bd. 15, S. 281.

as is usually observed where it is induced by the action of alcohol; but we are, nevertheless, justified in affirming that the syphilitic affection of the liver occasionally makes its appearance, if not in an uncomplicated form, at least, so far as regards its essential features, as cirrhosis.

As to the connection of cirrhosis with *intermittent fever*, this has not been noticed by German observers. It would appear, however, that, according to their views, it is but very seldom that the influence of malaria manifests itself in this manner upon the liver. Notwithstanding the great frequency of fever and ague at Breslau, Frerichs saw (*vide* Klinik der Leberkrankh., Bd. I., S. 364) but five cases of cirrhosis occurring after persistent intermittent fever, one other instance coming under his observation in Kiel (loc. cit., Bd. II., S. 67); and of these two were possibly induced by the abuse of spirituous liquors. Of fifty-one patients of Bamberger who were the subjects of cirrhosis, in only three had there previously existed obstinate intermittent fever. Upon the other hand, as is stated by Franco,[1] Cantani, of Naples, is of the opinion that cirrhosis of the liver, in Italy, where it is of very frequent occurrence, is not to be attributed to the abuse of alcohol, but that its essential etiological factor consists rather in the malaria-infection. Among the structural changes of the liver which are encountered as sequelæ of malarial fever, chiefly in tropical and sub-tropical countries, but also in intensely malarial districts in the temperate zone, A. Hirsch[2] describes a form of atrophy resembling cirrhosis due to obliteration of the vessels.

Botkin[3] has of late attempted to demonstrate a much more extensive connection between cirrhosis and pre-existing infectious diseases. He claims, moreover, with respect to *cholera* and the various forms of typhus fever, a direct influence upon the origin of this hepatic affection. According to his view, the anatomical lesions of parenchymatous organs (liver, spleen, kidneys, heart), when subjected to the influence of acute infectious pro-

[1] Il Morgagni, 1870. Virchow-Hirsch's Jahresb. 1870. Bd. 2, S. 1870.

[2] Hdb. der histor.-geogr. Pathol., Bd. 2, S. 321; compare ibid., S. 306.

[3] *Tschudnowsky*, Berl. klin. Wochenschr. 1872. Nr. 22. *Botkin*, Die Contractilität der Milz und die Beziehung der Infectionsprocesse zur Milz, Leber u. s. w. Berlin, 1874.

cesses, become in course of time the principal cause of chronic inflammatory processes in those organs.[1] It very seldom happens, he says, that we are able to trace the direct transformation of an infectious disease into chronic inflammation of the liver. The occurrence of such a transformation is, however, attested, in a majority of cases, by the history of an obvious causal relation with some pre-existing affection of that class.

The observations upon which Botkin bases this theory have not been communicated[2] by him. Moreover, in comparing numerous observations reported by other writers, it is extremely seldom that we find any allusions to previous ailments that would give adequate support to this view.[3] Nevertheless, the discussion raised by Botkin will, at all events, tend to stimulate further study of this interesting, and in a prophylactic sense important, subject. Inquiry should be directed particularly to the point whether, in those cases where the hepatic affection is in all probability to be traced to a pre-existing infectious disease, some other collateral agencies may not have contributed toward its development.[4]

Among the diseases caused by the reception of poisons into the system, in protracted cases of which the interstitial tissue of the liver not unfrequently undergoes alterations which may be identified with the commencement of the process giving

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[1] A similar theory will be found intimated by *A. Beer*, Die Eingeweidesyphilis. S. 158.

[2] The articles of *Tschudnowsky* relate only to the microscopical appearances found in the livers of ten patients who died of cholera, in *Botkin's* clinique; these all exhibited, in addition to changes of another character, the commencement of interstitial inflammation. The same appearances are described as observed in the livers of patients dying of typhoid fever. On the other hand, no case is cited in which well-developed cirrhosis of the liver was shown to be a consecutive affection to cholera or typhus fever.

[3] A case is reported, for instance, by *Redenbacher*, where in a woman, thirty-eight years old, the subject of cirrhosis, nothing could be gathered from the previous history beyond the fact that three years before the appearance of the ascites she had experienced an attack of cholera.

[4] In view of the statement of *Bleeker* (La Dysenterie, etc., La Haye, 1856, p. 21), that dysentery in the Indian Archipelago is most frequently complicated with hyperæmia and "*altération granuleuse*" of the liver, tropical dysentery also is possibly to be included among those infectious diseases, consecutively to which cirrhosis may be developed.

rise to cirrhosis, in addition to alcoholism mention should also be made of *phosphorus-poisoning*. This identification has been rendered more certain by the circumstance that G. Wegner[1] has succeeded in producing in animals (rabbits, cats, dogs) by the introduction of gradually increased doses of phosphorus an interstitial hepatitis, which, after the administration, continued for several months, of relatively large quantities of the poison, was transformed into granular atrophy, and occasioned death by precisely the same disturbances as are induced by the disease in human beings. The affection has not yet been observed, however, in man as the result of phosphorus-poisoning.[2]

That cirrhosis may be also developed as a form of visceral gout resulting from the gouty dyscrasia, as has been maintained even up to most recent times by English and French authors, is not probable;[3] for it neither occurs with remarkable frequency in patients the subject of gout, nor is it, in their case—like *nephritis arthritica*—attended by deposits of uric acid salts in the diseased organ.

With regard to the greater number of the deleterious agents already enumerated which may form the cause of cirrhosis, there is little question that they make their way into the liver together with the blood of the portal vein. This is shown by the nature of these noxious agents, as well as by the fact that the hepatitis induced by their action has its starting-point and principal seat in the vicinity of the smallest ramifications of the portal vein.

That closure of the hepatic vein can also entail cirrhosis of the liver was first of all established by Gintrac[4] and Oré[5] (by the latter from the results of experiments on dogs). Botkin[6] arrived

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[1] Virchow's Archiv. Bd. 55, S. 18.

[2] The notion of *Aubry* (Gaz. des Hôp., 1865, p. 113), that cirrhosis of the liver may be induced by chronic lead-poisoning, finds no sufficient confirmation in the cases reported by him.

[3] Compare, for instance, *Trousseau*, Medic. Klinik, German translation, Bd. 3, S. 283; and *Murchison*, On Functional Derangements of the Liver, London, 1874, p. 81.

[4] Jour. de Bordeaux. Jan.–Mars, 1865. Schm. Jahrbb. Bd. 93, S. 48.

[5] Fonction de la veine-porte. Bordeaux, 1861. Abstract of the same by *Robin*, Jour. de l'Anat. et de la Physiol. I., p. 556.

[6] Virchow's Arch. Bd. 30, S. 456.

at the same conclusion, in consequence of an observation where the appearance of a very rapidly increasing ascites preceded by several months the hepatic enlargement. By the other writers, on the other hand (Frerichs, Bamberger, Tuengel, Klebs, and others), wherever cirrhosis and occlusion of the portal vein are coexistent, the latter is invariably regarded as the result of the former. Quite recently Solowieff[1] has concluded, from experiments instituted by him on dogs, that the closure of the *vena porta*, when this takes place gradually, becomes in itself a cause of the development of a more or less extensive interstitial process in the liver, that can in no respect be distinguished from the cirrhotic process. In common with Botkin, he attempts to attribute the mode of origin of this lesion to the circumstance that after the closure of the trunk of the portal vein the connective tissue accompanying its ramifications is compressed neither by the blood-vessels, that are no longer filled to the former extent with blood, nor by the hepatic cells, that are undergoing gradual atrophy, and is, therefore, in the condition most favorable for proliferation. In the experiments of Solowieff, however, not only was the portal vein occluded, but also the calibre of its finest twigs was plugged with a finely granular mass, in consequence of which it is extremely probable that the blood from the hepatic artery also failed to reach the acini, while the blood-pressure in the nutrient vessels of the inter-acinous tissue was increased. The occlusion of the portal vein tends, of itself, to give rise neither to atrophy of the hepatic cells nor to development of interstitial connective tissue, proof of which is afforded by the cases of simple thrombosis of the portal vein in human beings.[2]

Finally, it should also be observed that granular induration of the liver occasionally appears as supplement to *chronic peritonitis*, the inflammatory process extending from the serous coat and Glisson's capsule to the interlobular structure.

As is indicated by the preceding statements, the causes of cirrhosis are quite manifold. To the majority of these causes attention has not been drawn until within a short time, which will

[1] Virchow's Arch. Bd. 62, S. 195.

[2] Compare, for instance, the observations of *Cohn*, Klin. d. embol. Gefässkrankh., S. 498, and of *Leyden*, Berlin. klin. Woch., 1866., Nr. 13., Beob. 2.

serve to explain the circumstance, that among the instances contained in the literature of the subject there are quite a number in which no etiological factor was discovered: these belong, for the most part, to that period when only the influence of alcohol upon the origin of the disease was accurately understood.

The *predisposition* appears to be decidedly greater in middle life and in the male sex.

Of Bamberger's patients, one-half were between the ages of 30 and 45; of Frerichs', 20 (of 36) were between 50 and 70; 12 between 30 and 50 years old. Of Bamberger's cases, 39 were men, 12 women; of Frerichs', 20 were men, 16 women; of Tuengel's, 24 were men, 6 women. In the Berlin Pathological Institute there were found, according to G. Foerster, among 3,200 autopsies, 31 cases of cirrhosis in individuals between 30 and 90 years of age, of whom 16 were between 40 and 60 years old; 24 were men, 7 women.

In old age, as well as in early childhood, we find very few patients. The youngest patient of Bamberger was fifteen years old. Gerhardt, in his Lehrbuch der Auscultation und Percussion (2. Aufl., S. 322), gives an account of a lad, aged fifteen years, addicted to liquor, and the subject of cirrhosis. Steffen observed the disease in a girl aged thirteen years, and in a boy of eleven years; Wunderlich, in two sisters of twelve and eleven years of age; Maggiorani,[1] in a boy of eleven years; Frerichs, in a boy of ten years; Loeschner,[2] in a girl of nine years; Hauerwaas, in a boy of eight years. I have not found in the literature of the subject any cases occurring at an earlier age,[3] with the exception

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[1] Gaz. clin. dello Sped. civ. di Palermo, 1874; *Mazzio*, Jahresbericht von Virchow u. Hirsch für 1874, Bd. 2, S. 259.

[2] Oesterr. Zeitschr. für Kinderheilkde. Jahrg. 1 (1856), Mai.

[3] The four cases of cirrhosis in children, reported by *Rilliet* and *Barthez* in the first edition of their work, are not to be found in the second edition. The case of a girl, aged four years, described by *Henoch* (in his edition of Budd's Monograph, S. 154), presents conditions varying in manifold particulars from those of cirrhosis (intense icterus, smooth and even surface of the liver, succulent condition of the interstitial tissue notwithstanding remarkable atrophy of the organ). According to the observations of *W. H. Dickinson* (Med. Chir. Transact., Vol. 52, p. 359; Schmidt's Jahrbb., Bd. 154, S. 284), an affection of the liver occasionally appears in early childhood, where rachitis exists, which appears to correspond to the first stage of cirrhosis.

of two observations of fœtal cirrhosis. One of these instances, that of F. Weber,[1] relates to a still-born twin; the other, that of Virchow,[2] to a child that died immediately after birth; in both the etiology was obscure.

Immoderate indulgence in brandy exercises, at all events, a material influence upon the conditions under consideration: cirrhosis and dipsomania essentially coincide in the frequency of their occurrence as regards age and sex; and the greater prevalence of the affection in the lower classes and in certain countries (England, North Germany) is in all probability to be thus explained. Leaving out, however, those cases induced by alcohol, the remainder would not be equally divided among all ages and both sexes, as may be seen from the statistics collected up to the present time, which no doubt are, upon the whole, very meagre: among the cases recently described as occurring in childhood[3] it is only the two of Wunderlich, that of Gerhardt, that of Hauerwaas, and that of Maggiorani, that are to be charged to brandy; but the others represent so small a number that they furnish sufficient proof of the absolute rarity of the affection as regards children.

Pathology.

General Features of the Disease.

The commencement of the affection is not usually characterized by any symptoms, and the first stage of its development runs its course without attracting notice. In exceptional instances only—generally in immoderate drinkers—for a period of months, and even years, before the outbreak of characteristic symptoms, dull or violent pains are experienced in the region of the liver, associated with tumefaction of the organ, gastric disturbances, and frequently also icterus and fever. Such an

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[1] Beitr. z. patholog. Anat. d. Neugebor. 3 Lief, S. 47.

[2] Virchow's Arch. Bd. 22, S. 426.

[3] In Virchow-Hirsch's Jahresbericht for 1876 five additional cases are also reported that were observed in children from six to twelve years old; in one only of these could the abuse of spirituous liquors be demonstrated as the cause.

attack commonly lasts only for a period of days; it may, however, frequently recur, leaving behind each time an increase in the hepatic enlargement; to the above are then gradually superadded other symptoms of the disease; or there may supervene after one or several attacks a long interval, during which the pathological process in the liver gives rise to but very trivial complaint, if any at all.

In the great majority of cases symptoms do not generally make their appearance until consecutive disturbances in other organs have already been produced. The disease is usually ushered in by symptoms proceeding from the stomach and intestines, such as impairment of the appetite, sensation of pressure in the epigastrium after ingestion, nausea, inactivity of the bowels. There almost invariably follows very speedily the commencement of a cachexia, which manifests itself by a pale or dirty yellow look, and the gradual emaciation and increasing weakness of the patient. Simultaneously with the above ascites usually appears, and after this, sooner or later, anasarca often supervenes, beginning in the feet. At this time the liver is, as a rule, reduced in volume, the spleen enlarged. The derangement of the digestive functions continues, although the appetite may often become improved. In certain cases hematemesis follows, and also hemorrhage from the intestines. Not unfrequently the constipation is subsequently changed into diarrhœa. Meteorismus and increasing ascites impede respiration. With the increase of the dropsy the urine becomes more scanty and relatively richer in pigment and urates. The pulse, which slowly diminishes in fulness and tension, does not usually become accelerated until toward the end. Decided icterus rarely appears during the course of the disease. More frequently there are observed at a later period petechiæ upon the skin and hemorrhages from the nose, gums, etc. Occasionally severe cerebral symptoms ultimately set in. Death commonly ensues from pulmonary œdema or collapse, after the patient has become extremely emaciated and debilitated, or after some acute affection has supervened. Complications may occasion death even in an earlier stage of the disease while the volume of the liver is still enlarged.

Anatomical Changes.

In the majority of cases the cirrhotic liver is found on post-mortem examination reduced in size, and attached by means of funicular or membranous pseudo-ligaments to the adjacent organs, especially to the diaphragm. The reduction in size is often but slight, at other times more considerable, reaching to such a degree that the volume of the organ amounts to scarcely one-half the normal. The weight is not diminished in a corresponding ratio, and, when the reduction in volume is but moderate, may even be somewhat above the normal point; in case of very great atrophy, it may sink as low as 1,000 grammes, or thereabouts. The reduction is usually most strikingly manifested in the left lobe, which now and then appears as merely a slender membranous appendage of the right. In the right lobe, too, the sharp margin is not unfrequently transformed into a thin, flabby rim, which is folded over forward or backward, and may be fastened in this position by means of false ligaments; but, ordinarily, the right lobe is diminished more in height and breadth than in thickness. The outer surface of the liver is rendered uneven by numerous nodules and knobs, which show a yellow color through the capsule, that is more or less thickened and at times studded with villi, and which are separated from one another by whitish gray depressions. These so-called granulations form usually semi-globular prominences, varying in size from a millet-seed to a pea; sometimes they are all of nearly a uniform, and at other times of an unequal size: ultimately they may here and there attain the size of a hazelnut, and are then occasionally of a grape-like form. The structure of the granulated liver is very firm, amounting to an almost cartilaginous consistence; upon section it emits a grating sound, is of a leathery toughness, dry, and anæmic. The appearance upon section corresponds to the outwardly visible alterations; a whitish gray network of lines unequal in breadth, usually sharply defined, composed of firm connective tissue, exhibits in its interstices roundish or irregularly-formed islets of parenchymatous tissue, corresponding in size to the projecting knobs on the surface, and usually of a deep yellow, rarely of a yellowish brown

or greenish color. These parenchyma-islets project more or less conspicuously above the surrounding substance, as the callous tissue between them retracts from the cut surface. We detect, even with the naked eye, in the fine streaks of connective tissue which branch out from the broad framework of the indurated tissue, and invest the granulations, as well as in the acinous structure of the latter that is usually invisible, that these islets are not composed each of a single lobule, but of a small or large number of lobules. The portal vein and the hepatic artery, as well as the larger branches of both vessels, are not unfrequently dilated. The tissue of Glisson's capsule in relation with these large vessels, is not, as a rule, thickened. Moreover, the macroscopic bile-ducts present nothing abnormal. The contents of the gall-bladder are frequently thinner, paler, and more scanty than the ordinary bile.

The appearances above sketched correspond to those observed in the most advanced cases; but the picture presented by the liver, when death takes place in an earlier stage of the disease, differs from this in many respects. The organ is then almost constantly and indeed often to a considerable extent enlarged, and may weigh as much as 3,000 grammes. Its form does not vary essentially from the normal; though sometimes the increase in volume of the left lobe is more notable than that of the right. The organ presents, upon the whole, a considerably increased consistence. The outer surface is smooth and for the most part apparently of a uniformly yellow hue. Upon more careful inspection, however, there may be distinguished, even upon the outside, and still more plainly upon the cut surface, the parenchyma-islets, colored more or less intensely yellow, and the pale rose-red or gray-red intervening tissue. The latter is considerably thickened, often to such an extent that it seems to exceed in mass the glandular substance; it forms net-like, ramifying streaks, which penetrate deeper between the lobules than the normal interlobular structure, and apparently completely encircle groups, larger or smaller, of these lobules. Sections in various directions show, however, that these lobular groups are not completely isolated, but that they maintain always, upon one side at least, connection with others.

The transformation from the condition of the liver just described to that first depicted, is represented in those cases where the volume of the indurated organ is still enlarged, or not yet reduced below the normal, but where there is plainly exhibited in spots (upon the left lobe and along the free margin of the right) or over the entire organ the process of granulation. Here, also, it often happens that the fibrous tissue between the granulations does not yet present the gray-white appearance of cicatricial tissue, but a gray-reddish color.

The seat of the pathological process, by means of which the changes peculiar to cirrhosis are brought about, is the interlobular connective tissue. Whether the liver is enlarged or reduced in volume, there is invariably found in this tissue, along the margin of the lobules, an infiltration of round and spindleform cells, varying in amount at different points. This infiltration is usually most abundant in the vicinity of the finest ramifications of the portal vein, and may be followed out at points along the capillary vessels as far as the peripheral zone of the lobules. A portion of the cells of this infiltration is developed into a fibrous texture, very rich in fixed corpuscles, which by shrivelling come gradually to resemble firm cicatricial tissue. Another portion of the cells is in all probability to be regarded as the first installment of newly-developing vessels branching out from the capillaries of the interlobular arterioles. For, as Frerichs first pointed out, we can inject from the *arteria hepatica* in the thickened connective tissue of the cirrhotic liver, a network of inter-anastomosing capillaries of comparatively large calibre, which, from their arrangement and the peculiar character of their walls, may be distinguished as of recent formation. That new vessels shoot out from the ramifications of the portal vein, as Virchow seems to think, cannot be perceived in the engravings of his injected preparations, and is, moreover, in itself improbable. The terminal branches of the portal vein, in consequence of the shrivelling of the newly-formed connective tissue with which they are surrounded (possibly also in consequence of the proliferation of this substance, Liebermeister), suffer a compression, as a result of which they become obliterated. This involves the destruction of those hepatic lobules that are nourished by these

branches of the portal vein. For, as has been demonstrated by Cohnheim and Litten,[1] not only the blood from the portal vein, but also that from the hepatic artery penetrates—the greater portion at least—through the interlobular veins to the capillaries of the lobule. If these veins become impervious, then all appreciable afflux of blood to the lobule ceases; its capillaries are destroyed and the hepatic cells become atrophied. Before the experiments of Cohnheim-Litten were made known, the destruction of the lobules was explained upon the theory of an intralobular proliferation of connective tissue. This view appears to be supported by the circumstance that we frequently see in the peripheral portion of the lobule atrophied groups of hepatic cells, or fragments detached therefrom, separated from one another by broad streaks of fibrous tissue, while the central portion exhibits cells still well preserved and normally arranged. Inasmuch, however, as each hepatic lobule is supplied with blood by more than one interlobular vein, such a partial atrophy might also be attributable to the fact that the affluent vessels are not altogether obliterated. It is indeed quite possible, however, that both processes—the obliteration of the interlobular veins, and the occlusion of the peripheral capillaries by intralobular proliferation of connective tissue—may play a part in producing the atrophy of the glandular parenchyma. In the callous tissue that appears in place of the latter, there may be often seen fine particles of fat, and small accumulations of yellow or brown pigment, forming the final residuum of the destroyed hepatic cells. The interlobular bile-ducts survive the destruction of their respective lobules; the extended double rows of their cubical epithelium, branching out at times dichotomously, are very numerous in the fibrous mass.

Those portions of the glandular parenchyma which remain intact until the last, form projecting granulations upon the outside and upon the cut surface. Their hepatic cells rarely present a perfectly normal appearance. In many cases they are enlarged by compensatory hypertrophy, often to twice or three times the

[1] Virchow's Archiv. Bd. 67, S. 153 f.

normal size (Klebs). They are usually rich in bile-pigment, which is accumulated in fine granules, or which may also impart a uniform color to the entire protoplasm. Inasmuch as this icterus is limited, as a rule, to the granulations, its origin must be referred to the circumstance that, owing to the proliferation of connective tissue at the edge of the lobules, the discharge of the secretion from the bile-capillaries into the interlobular ducts is impeded. An abundant quantity of fat remaining within the hepatic cells usually contributes, moreover, toward the yellow color of the granulations. These cells frequently present precisely the same appearance as in chronic fatty degeneration of the liver. Although this condition may be occasionally due to the action of some one of the well-known pernicious habits which tend to induce an immoderate deposit of fat in the liver—such, for instance, as the abuse of alcoholic spirits—it nevertheless undoubtedly originates still more frequently in the circumstance that, since the total number of the hepatic cells is materially diminished, of the fat deposited in a quantity not of itself abnormal, a larger proportion falls to each of the cells. At other times, the circumstance that in addition to the hepatic cells filled with oil-globules, some also are to be seen presenting simple granular clouding of the protoplasm, leads to the conclusion that fatty degeneration is present, to be attributed possibly to the insufficient afflux of blood from the interlobular veins reduced in calibre by the cirrhotic process. At times the parenchyma of some or all of the granulations exhibits the changes characteristic of acute yellow atrophy of the liver. Nothing abnormal is presented, as a rule, by the capillary network of the lobules, except the deposit of round and spindle-form cells in its peripheral portion, as above described. When, in exceptional instances, the capillaries have been found to be dilated, this was referable to an obstruction of blood in the hepatic veins, produced by some complication with valvular disease of the heart, for example, as in the Observation of Cornil (loc. cit., p. 274).

As follows from the above, the pathological process which takes place in cirrhosis of the liver may be characterized as diffuse, chronic inflammatory hyperplasia of the interstitial con-

nective tissue, and consecutive shrivelling of this hyperplastic structure. The former leads to enlargement of the organ in the earlier, the latter to the reduction of its volume in the later stages of the disease. It would be incorrect, however, to designate the first stage of the disease as that of hyperplasia, and the second as that of contraction. Except at the very commencement, during the entire course of the disease, hyperplasia and contraction are coexistent. As long as the structure undergoing development exceeds that which has become atrophied, the liver is enlarged; if the reverse condition appears, it is reduced in volume. Under certain circumstances, also, the condition of the glandular parenchyma contributes to the increase of volume: this is the case when, in addition to the interstitial inflammation, a high degree of fatty infiltration or of amyloid degeneration exists. In the latter combination, especially, the liver may become exceedingly large and heavy—(Ilmoni[1] describes a case of this character where the organ weighed nineteen pounds)—and, even after the shrivelling has become quite extensive, may still remain enlarged. That the contraction leads, as a rule, to a diminution in the bulk of the liver, is due in part only to the reduction in volume of the newly-formed connective tissue itself; otherwise, and to a greater extent, it is attributable to the atrophy of the glandular parenchyma induced by the retraction of this tissue.

In the cirrhosis of Laënnec the interstitial hepatitis is diffused, indeed, throughout the entire organ, but not in uniform degree; numerous groups of lobules, both large and small, remain intact, while others, situated between them in the fibrous texture, undergo destruction. The cause of this unequal distribution of the inflammatory hyperplasia has not yet been ascertained. The theory of Charcot and Gombault, that it is not the interlobular veins, but the next largest ramifications of the portal vein—those corresponding to the sub-lobular veins of the liver (*les vaisseaux veineux portes prélobulaires*)—from which the development takes its origin, is not supported by anatomical proof.

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[1] *Ilmoni* und *Toernroth*, Analecta clin. icon. illustr. Helsingförs, 1851. Tab. 4.

Symptomatology.

The opportunity is rarely afforded of following step by step, as has been done by R. Bright, the incipient swelling of the liver and its gradual diminution in volume. In most cases patients, when they seek aid, are already in a late stage. In exceptional cases, however, the first development of the affection is attended with great suffering; or it may be that complications with other diseases of the liver, or intercurrent affections of other organs, serve to bring an earlier stage under the physician's observation. The liver appears then enlarged, at times so considerably as to give rise to perceptible bulging of the abdomen; it may extend as far as the umbilicus, and even beyond the middle point between this and the symphysis (as, for instance, in a case of Liebermeister, loc. cit., S. 59, Beob. 13); its outer surface feels smooth and quite resistant; its lower margin is, likewise, firm and also sharp, but thicker than normal; the *incisura interlobularis* is often quite perceptible.[1]

This comportment of the liver, corresponding to the hyperplasia of the interstitial connective tissue, changes with the increasing shrivelling of this texture. In proportion as the enlargement gradually recedes, the lower margin of the organ approximates more and more the upper. As the left lobe is, as a rule, at first abnormally small, every trace of dulness between the right lower margin of the ribs and the ensiform cartilage is not unfrequently absent, whereas in the vicinity of the right lobe the area of dulness is still normal, or even abnormally great, and the resistance to be felt upon percussion is increased. But even here the region of dulness may be ultimately reduced to a

[1] According to *Borelli*, it is characteristic of interstitial hepatitis that the upper boundary of hepatic dulness, even during the incipient enlargement of the organ, is moved upward, and usually maintains this high situation during the further progress of the disease. The causes of this condition are referred by *Borelli* partly to the meteorismus which may be present even at an early stage, preventing the extension of the liver downward, partly to paresis of the diaphragm induced by the consecutive perihepatitis. This elevated position of the liver is, however, by no means so constant a symptom of the first stage of the disease as is alleged by *Borelli*, by whom it was, indeed, found each time in sixteen cases observed by him in the "neoplastic phase."

narrow strip, which, in the papillary line, extends over only from two to three ribs. The reduction in volume of the cirrhotic liver proceeds, as a rule, slowly; in exceptional instances only does it make such rapid progress as in the case observed by Stricker, where the vertical diameter of the dulness in the parasternal line diminished within a month from twenty-four to eleven centimetres. When the shrivelling has attained such a degree that the right lobe, also, has been reduced below its normal volume, it often happens that the size of the organ cannot be at all determined, because it is forced upward and backward, or covered by folds of the intestines pushed upward by the ascites, and usually, moreover, still inflated. The ascitic fluid itself may also cover a portion of the liver, in consequence of which the dulness thereby produced merges into the hepatic dulness with no appreciable boundary between the two; then the diminution of the organ in size can often be made out by means of percussion while the patient is lying upon the left side; at other times this is possible only after paracentesis. The margin, if accessible to the fingers when forced beneath the arch of the ribs, usually appears thin and sharp, or it may even be folded over; now and then a number of granulations may be felt in the form of small prominences, which vary in size from that of a lentil or pea, to a grape, and, in rare cases, form here and there well-marked projecting groups. Where, in consequence of the combination with amyloid degeneration or considerable fatty infiltration of the liver, there still exists enlargement of the organ, even though the contraction is far advanced, there then may be detected through the thin and relaxed abdominal integument, and by palpation combined with tapping, even through a layer of ascitic fluid, the finely nodulated condition, extending at times over the entire portion of the anterior surface that projects below the margin of the ribs: the granulations of the liver are distinguishable from similar projections having their seat in the abdominal wall and composed generally of collections of fat, by their upward and downward motion accompanying inspiration and expiration, which in very rare instances only is altogether arrested by firm adhesions with the parietal peritoneum.

At points where the cirrhotic liver lies in contact with the abdominal wall there may often be felt, and with the aid of the stethoscope heard, a friction or grating sound caused by the displacement of the parts, which may be induced by respiration or by stroking with the fingers (Jackson,[1] Bamberger,[2] Seidel[3]). This sound is due to the roughness of the respective peritoneal surfaces produced by the perihepatitis.

As long as the organ is enlarged it appears, as a rule, somewhat sensitive to strong pressure, and also gives rise frequently to a sensation of heaviness and tension in the right hypochondrium. In exceptional cases, occurring chiefly in topers, there appear in the commencement of the disease severe periodical pains in the region of the liver, accompanied with great tumefaction of the organ, and usually also with fever. Such attacks, which are wont to last some days, may be frequently repeated, sometimes at regular, at other times at irregular intervals. We have here to deal, in all probability, with fluxionary hyperæmias, such as are also otherwise produced in this class of individuals by dietetic irregularities, especially by excess in drinking. During the subsequent course of the disease there is, as a rule, no sensitiveness in the hepatic region; where this exists temporarily, it is due to an exacerbation of the perihepatitis.

The obliteration of numerous interlobular veins by the shrivelling connective tissue causes a material obstruction to the blood-current in the portal vein. The lateral pressure in the branches, the trunk, and roots of this vessel is correspondingly increased. This increase in the blood-pressure is propagated in those veins also which form, outside the liver, communication between the portal system and that of the *venæ cavæ*, and not unfrequently gives rise to a more or less decided dilatation of those veins, which serve then as outlets for the obstructed portal blood. The channel most suitable for this purpose is a vein inside the *ligamentum teres*, and running almost its entire

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[1] American Journal of the Medical Sciences. July, 1850. Schmidt's Jahrbb. Bd. 69, S. 329.

[2] Kkhten. d. chylop. Syst. S. 516.

[3] Deutsche Klinik. 1865. Nr. 49. Beob. 5.

length, which receives from the abdominal wall several sub-peritoneal twigs, and discharges into the left portion of the *sinus venæ portæ*. As has been recently demonstrated by P. Baumgarten,[1] this vein forms the remaining portion of the canal of the imperfectly obliterated *umbilical vein*, which in most human beings continues pervious during entire life. This is oftentimes (in eight out of sixty cases) so broad that one can readily introduce into it a thin or thick steel sound, and in cirrhosis of the liver it may become dilated to the size of a goose-quill, and even of the little finger.

The very large vein in the *ligamentum teres*, observed in many cases of cirrhosis, was even long ago regarded as the redistended umbilical vein, the theory being that the obliteration of the latter, ordinarily complete, had, by way of exception, not taken place in the individuals in question. Sappey (Bull. de l'Acad. d. Sc. méd., T. 24, p. 943, Juin, 1859) showed this view to be erroneous, since the umbilical vein invariably remains open only a short distance from its portal end, but elsewhere is obliterated so as to form a solid cord; what has been mistaken for it is one of the vessels described by him as *venæ portæ accessoriæ*, which discharges into the left branch of the portal vein directly adjacent to the point of insertion of the umbilical cord. But Bamberger (Krankh. d. chylop. Syst., S. 520) long since asserted that he had frequently found the umbilical vein in adults pervious to a fine sound. Subsequently Hoffmann (Correspondenzbl. f. Schweizer Aerzte, 1872, Nr. 4) reported a case of cirrhosis where the vessel, eight millimetres in diameter, was demonstrated to be the umbilical vein by the fact that at the navel it communicated with the *vena epigastrica inferior*, in the portal fissure, with the portal vein, and through the open *ductus venosus Arantii*, with the inferior vena cava, no cord being found corresponding to the *ligamentum rotundum*. According to the experiments of Baumgarten, the *ductus venosus Arantii* belongs, likewise, to the imperfectly obliterated fœtal vessels; the remaining portion of its canal was found also by this observer in a case of cirrhosis, where the umbilical vein was somewhat distended, to be somewhat larger than usual.

Through the distended umbilical vein the blood flows with a reversed current from the portal vein to the abdominal wall, the deep veins of which are consequently thereby uniformly dilated. As the stagnation is propagated therefrom to the subcutaneous abdominal veins, the latter may be distended into large vessels from one-half to one centimetre in transverse diameter, which project as highly tortuous, bluish ridges beneath the

[1] Centralbl. f. d. med. Wiss. 1877. S. 722–725 u. 741.

skin. These then form a plexus that surrounds the umbilicus in the form of a wreath or star (cirsomphalus, caput Medusæ), or extends upon both sides of it upward as far as the epigastrium and over the anterior surface of the thorax, and downward toward the inguinal region. Now and then there may be detected by the outspread hand a gentle whirring, and by the aid of the stethoscope a continuous rustling over these varicose veins (Bamberger,[1] Sappey). Outlets are opened for the blood of the *ramifications of the portal vein*, partly by the dilatation of the veins running through the *ligamentum suspensorium* and *coronarium* from the diaphragm to the liver (Sappey), partly through the newly-formed vessels of the perihepatic pseudomembrane, which furnish communication between the distended capsular veins and the *venæ diaphragmaticæ*. Next to the *ramifications of the portal vein*, according to a widely accepted theory, it is principally the *vena hæmorrhoidalis interna* that serves to *draw off the blood into the vena hypogastrica;* but however much this appears to be favored by its numerous anastomoses with the venous plexus of the lower extremity of the rectum, yet varices do not occur with especial frequency in the latter in case of cirrhosis, as has already been pointed out by Sappey and Frerichs. Still less frequently has a dilatation been observed in other veins which lead directly from the walls of the intestinal canal to the system of the *vena cava;* Rindfleisch[2] observed in one case, in addition to obliteration of all the ramifications of the portal vein, a number of quite dilated anastomoses of the mesenterial veins with the spermatic veins. On the other hand, the varicose dilatation of the *venæ œsophageæ inferiores*, by which the discharge of blood from the *vena coronaria ventriculi* to the *vena azygos* is maintained, first observed by Fauvel (Gubler, loc. cit.), has been repeatedly seen in recent years.[3]

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[1] Wiener med. Wochenschrift. 1851.

[2] Lehrbuch der patholog. Gewebelehre. 3. Aufl., S. 429.

[3] *Ebstein*, Schmidt's Jahrbb. Bd. 164, S. 160. *Audibert*, Des varices œsophagiennes dans la cirrhose du foie. Paris, 1874. *Hanot*, Étude sur une forme de cirrh. hypertroph. du foie. Paris, 1876, p. 19. Compare further this Cyclopædia. Bd. VII., 1. Anhang, S. 127 f. (Vol. VIII. of American edition.)

Although collateral circulations of this sort, especially at points where they cannot be recognized during life, are possibly somewhat more frequently to be found upon careful examination of the cadaver than appears from previous observations to be probable, yet it is only in extremely rare instances that they prove sufficient for the complete and permanent relief of the portal system. As may be readily seen, this result will be most likely to be attained when they form direct communication with the trunk itself, or with the intrahepatic twigs (*vide* examples under Ascites). As a rule, however, the obstruction to the circulation existing in the liver gives rise to more or less stagnation in those organs which send their blood to the portal vein. There are thus produced in the liver, diaphragm, stomach, and intestinal canal, venous hyperæmia and further changes resulting from this lesion.

The *spleen* is in most cases *swollen.* If the experience of many authors seems to contradict this statement, this is to be explained by accidental circumstances which even the relatively extensive observations of any single physician are not sufficient to exclude. If we add up the observations of Bamberger, Oppolzer, Frerichs, E. Wagner, Birch-Hirschfeld, and those from the Berlin Pathological Institute reported by G. Foerster, there will be found out of 172 cases only 39 (or between 22 and 23 per. cent.) in which the splenic tumor was absent. As a rule, the enlargement attains only from one and a half to three times the natural volume, and even then not unfrequently escapes observation, when the organ is pushed far upward and backward beneath the left lung by severe meteorismus; but now and then it becomes much more considerable, and forms a firm tumor, which may project downward as far as the vicinity of the navel, and even below this point. The increase in volume is by no means invariably proportionate to the degree of the obstruction; for it is only in part produced directly by the venous engorgement. It depends usually, so far as concerns its essential feature, upon a diffuse hyperplasia of the splenic tissue.[1] This often originates

[1] Compare *Eichholtz*, Mueller's Archiv. 1845. S. 335. *Virchow*, Wiener medic. Wochenschrift. 1856. S. 534. *Liebermeister*, Beiträge. S. 132.

no doubt, from the influence of the hyperæmia due to obstruction, and consequently appears as a sequence of the hepatic affection; but at other times it arises concurrently with the latter, the same irritants which excite the development in the interstitial tissue of the liver (malaria,[1] syphilitic poison,[2] and other infecting material) also giving rise to a proliferation of the elements of the splenic parenchyma. The splenic tumors formed in this manner are developed concurrently with the hepatic cirrhosis, and may be discoverable even before the latter has yet given rise to any appreciable disturbance in the circulation of the portal vein. But they are, of course, still further enlarged by the consecutive obstructive hyperæmia. The tumefaction of the spleen, in so far as it is dependent upon obstruction, varies with the degree of the latter; after profuse gastrorrhagia a sudden reduction in volume of the splenic tumor may often be detected. Where, owing to a considerable fibrous thickening, or calcification of its capsule, the organ is not susceptible of distention, or where, as not unfrequently happens in aged and decrepit persons, it is in a condition of atrophy,[3] there is then no enlargement.

In the later stage of the disease *ascites* is an almost constant symptom. The cases in which it is absent are principally those where, in consequence of some complication, death supervenes before extensive shrivelling of the newly-formed tissue has taken place. But if this contraction has already occurred, it is then extremely seldom that, by the development of a sufficient collateral circulation, the obstruction in the portal system leading to transudation into the abdominal cavity is avoided.[4] In the production

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[1] *Frerichs* (loc. cit., Bd. 2, S. 44) remarks that, in regions where intermittent fever frequently prevails, the splenic tumor seems to be conjoined with cirrhosis more frequently than in other localities.

[2] Vide *Virchow* in his Archiv. Bd. 15, S. 319. Compare further this Cyclopædia, Vols. III. and VIII.

[3] The circumstance that *Frerichs* failed to find the splenic tumor in 18 out of 36 patients, *Bamberger*, on the other hand, in only 4 out of 51, is to be referred perhaps, in part at least, to the difference in the relative age of the different patients under consideration; among those of *Frerichs* 21 were over 50 years old, while one-half of those observed by *Bamberger* were between 30 and 45 years of age.

[4] Thus, in a case observed by *Sappey*, where from ten to twelve veins of the *liga-*

of the ascites the increased blood-pressure in the vessels of the peritoneum constitutes, no doubt, the most important factor; but it is obvious that an influence is also exerted by the condition of the blood. Now, as the latter is often dependent, not upon the hepatic affection alone, but more or less also upon preceding or synchronous affections of other organs, it will be understood why the ascites makes its appearance in many instances at an early stage, at other times not till later. It may even precede all other symptoms of obstruction, and thus form apparently the first indication of the disease, while the patient's attention is not drawn to his disorder until the abdominal distention begins to disturb him. Corresponding to the gradual increase of the cirrhotic shrivelling, the ascites is usually developed slowly, but attains not unfrequently a considerable grade, such as is hardly observed in any other disease of the liver. Once present, as a rule, it does not again disappear. Where, in exceptional cases, it does subside, this is due to an unusual effect of certain therapeutic agencies (*vide* under Treatment) or to a diminution in the stagnation consecutive upon a dilatation of the collateral blood-channels (Monneret, Frerichs). Where, owing to watery diarrhœa or gastrorrhagia, the pressure in the tract of the portal vein is reduced, the transudation experiences, indeed, a temporary diminution; but afterward, in consequence of the greater anæmia, is increased all the more rapidly. Moreover, after puncture of the abdomen, which usually gives outlet to between twenty and forty pounds of fluid, the accumulation usually reappears perceptibly even after a few days, and within from two to four weeks —in patients very much reduced, within even a shorter period —is wont to attain its former height.

The ascitic fluid is clear, usually yellow; less frequently colored greenish or brownish by bile-pigment, or reddish by extravasated blood-corpuscles. Its chemical constitution does not differ essentially from that of the serous effusions of the peri-

mentum suspensorium, dilated to the size of a crow's quill, conducted the blood from the liver to the *venæ diaphragmaticæ;* furthermore, in the case of Hoffmann, above described, with distention of the umbilical vein; as well as in a case related by *Hanot* (Thèse de Paris, 1876, p. 19), with varicose dilatation of the *venæ œsophageæ*,—no trace of ascites was present.

toneum which occur in other diseases; it contains from 1½ to 3 per cent. of solid matters, of which, as a rule, more than one-half is albumen.

Redenbacher found in one case 1.333 per cent. solid constituents, of which 0.849 per cent. was albumen; F. Hoppe[1] found 1.55–1.75 per cent. solid matters, and 0.62–0.77 per cent. albumen; in six analyses by Frerichs the quantity of the solid constituents varied between 2.04 and 2.48 per cent.; that of the albumen from 1.01 to 1.34; Bamberger reports as the result of his analysis, 3.032 per cent. solid matters, of which 2.497 were organic; Budd, 3.015 solid matters with 2.251 albumen. In a case of Frerichs, of concurrent peritonitis of mild degree, the quantity of solid ingredients rose to 3.59 per cent. with 2.60 per cent. of albumen.

There was also detected among the constituents of the ascitic transudation in cirrhosis, fibrin; subsequently, in many instances, coagula (Frerichs); in several instances sugar (Frerichs, Bamberger); urea (Redenbacher, 0.077 per cent.; Bamberger, traces); leucin (Frerichs).

Within a variable period after the appearance of ascites, *œdema* of the feet is very often developed; in exceptional instances only does the dropsy, when not induced by some complicating affection of the kidneys or heart, appear simultaneously in both parts; and perhaps even then this coincidence is only seeming in so far as the commencement of the ascites more easily escapes observation than the superficial swelling. This œdema not unfrequently spreads further, implicating after a while the thighs, the external genital organs, the region of the intestines and loins, and the anterior abdominal wall. The upper half of the body, on the other hand, apart from complications with cardiac and kidney disorders, remains almost always intact, or at the most hydrothorax is ultimately superadded. The most frequent cause of the œdema is in all probability the effect of the intra-abdominal pressure upon the *venæ iliacæ* and the *cava inferior*, which is decidedly increased by the ascites and meteorismus. If this pressure is reduced by puncture, then the anasarca is usually diminished. Where the communications between the portal vein and the *vena epigastrica* have experienced great dilatation, the increased afflux which takes place from the latter

[1] Virchow's Archiv. Bd. 9. Heft 1.

to the *vena cruralis* may impede the backward flow of the blood from the lower extremities, and thereby give rise to the development in them of œdema, before a still higher degree of ascites is present. Under the same circumstances, the abdominal integument becomes at times at a still earlier stage œdematous (Monneret), the increased pressure being propagated to its veins from the epigastric vein, which in turn is over-distended from the portal vein. In exceptional instances a very considerable œdema of the entire lower half of the body is due to the circumstance that the *pars hepatica* of the inferior *vena cava* is subjected to a contraction by the shrinking of the liver (Bamberger). When the ascites has reached such a degree that the blood-current in the inferior *cava* is impeded by the very great tension of the abdomen, then the obstructed outflow from the veins of the abdominal integument not unfrequently results in a dilatation of their superficial ramifications. The vessels thereby becoming visible upon the abdomen are distinguished from the collateral phlebectases by their lesser volume and more extensive distribution; they are never limited to the vicinity of the umbilicus; on the contrary, they are developed principally in the lateral parts.

Symptoms referable to the stomach and intestines are very commonly present in cirrhosis. Where found even in the early stage, they proceed from morbid changes of the digestive organs produced by the action of the same pernicious influences (abuse of spirituous liquors, malaria) as is the hepatic disorder itself. It more frequently happens that they do not appear until a later period, and are then usually dependent upon nutritive and functional derangements developed in the walls of the digestive canal under the influence of prolonged obstruction of the blood. Now and then the appetite and bowels continue normal even to the end, which is due partly to the absence of the venous hyperæmia of the digestive organs in consequence of the diversion of the blood of the portal vein through collateral circulation, partly to individual conditions as yet unknown. But the greater number of patients suffer from *gastric derangements* and constipation; anorexia, nausea, feeling of tightness at the epigastrium, eructations after meals, etc., are experienced; the solid stools are covered with a layer of vitreous-looking mucus. Cor-

responding thereto are commonly found, on post-mortem examination, in the stomach and duodenum, indications of chronic catarrh. There are, nevertheless, other cases where these lesions are absent, although during life symptoms of dyspepsia have existed. This is perhaps attributable to the circumstance that the derangements produced by the ascites and tympanites tend to increase after each ingestion. So, likewise, the *inactivity of the bowels* originates not merely in the changes in the abdominal walls; it may also be due to the pressure exerted by an excessive transudation in the peritoneal sac upon the portions of the intestinal canal retained in the pelvis, as well as to the diminished afflux of bile; for in progressive atrophy of the secreting parenchyma the quantity of the secretion undoubtedly becomes, as a rule, gradually diminished. And, in fact, the intestinal excretions acquire very often an abnormally pale color in the later stages of the disease, even where no jaundice is present. Graves and Frerichs point out that now and then one portion of the fæces may be pale and clay colored, and the other darker; Bamberger and Jaccoud observed a variation between normally colored and pale stools. Still it not unfrequently occurs, however, that, notwithstanding appreciable diminution in the volume of the gland, the fæces continue normal in appearance. Possibly the deficiency arising from the great diminution of the hepatic cells is here in some measure compensated for by the hypertrophy of those surviving. The same agencies which serve to account for the constipation favor, moreover, the development of *meteorismus;* the most important factor, however, in producing this condition would appear to be the relaxation of the abdominal walls, attributable, no doubt, chiefly to the serous infiltration of the muscular tissue. In the later stage of cirrhosis meteorismus is almost uniformly present, and becomes often so considerable as to constitute the most annoying symptom of the affection. Toward the end of life, and frequently also even sooner, diarrhœa often sets in. This is, in all probability, induced principally by the dropsical transudation; as is often proved by the thin, watery consistence of the dirty pale-yellow, almost colorless evacuations, as well as by the œdematous condition of the intestinal mucous membrane frequently found in the cadaver.

It occasionally originates in the consecutive diphtheria of the rectum and colon. When amyloid degeneration of the liver is associated with the cirrhosis, then the similar affection of the intestinal mucous membrane may form the cause of the looseness. Profuse *hemorrhages* from the mucous membrane of the *digestive canal* (frequently, indeed, of the stomach, and more rarely of the intestine) occur chiefly when the ascites has attained such a degree, that further escape of serum from the peritoneal vessels is impeded by the tension of the abdominal walls, and consequently the stasis in the intestinal roots of the portal vein is augmented to a very considerable degree. Previous to the appearance of ascites, hæmatemesis not unfrequently occurs; which, in exceptional instances, may even constitute the first striking symptom of the disease.[1] As a rule, it is the over-distended capillaries, but in many instances, also, submucous varices, which burst. In addition to the exudation into the free surfaces, there frequently results, also (in stomach and duodenum), the formation of hemorrhagic infiltrations and erosions of the mucous membrane. Profuse vomiting of blood is, on the whole, no rare accompaniment of cirrhosis,[2] which gives rise more frequently than any disease, except simple gastric ulcer, to this symptom. In some cases this may be repeated several or even many times. Rollett[3] observed hæmatemesis recur during a period of two years almost regularly at intervals of from four to five weeks, after which the ascites, that had in the meanwhile reaccumulated, in each instance abated. Rarely the vomited blood proceeds not from the gastric vessels, but from a varix in the lower portion of the œsophagus that has been either ruptured or eroded by ulceration of the mucous membrane (*vide* p. 187).

Although the alterations of the interstitial tissue give rise constantly in the later stage of the disease to a more or less decided

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[1] *Heitler* (Wiener med. Presse, 1872, Nr. 30) reports such a case occurring in a woman thirty-six years of age. The same was observed by the writer in a well-nourished toper forty-seven years old.

[2] The reader will be struck by the contrary statement made by *Trousseau* (loc. cit., S. 421).

[3] Wiener med. Wochenschr. 1866. S. 99.

stasis of the portal blood, they never of themselves produce any very great stagnation of the bile; for, although the hepatic icterus usually existing renders it certain that the elimination of the secretion from that portion of the gland still surviving and performing its functions is not so completely unimpeded as in the normal condition, yet in the majority of cases universal *icterus* is observed either not at all, or, at most, in mildly developed form, as a light, yellowish discoloration of the superficial integument, limited now and then to the upper half of the body, while in the urine bile-pigment cannot always be detected. We are, therefore, forced to conclude that the smallest bile-ducts at the margin of the lobule are not rendered impervious by the shrinking of the newly-formed connective tissue until this shrinkage constricts also the interlobular veins, and thereby arrests the transportation to the hepatic cells of the material necessary for the elaboration of the bile. Where in the course of the affection a pronounced icterus appears, it is usually due to some consecutive complicating disorder of the *ductus choledochus*, such as catarrh of the *pars intestinalis;* compression at the *ligamentum hepato-duodenalis* by callous tissue, swollen portal glands, etc.: or it may be attributable to acute yellow atrophy of the surviving glandular parenchyma.

The remaining morbid symptoms proceed either as necessary sequelæ from the lesions already enumerated, or are dependent upon secondary processes and complications.

The progressive reduction in volume of the secretory parenchyma of the liver and the impairment to which the functions of the digestive organs are inevitably subjected by the venous hyperæmia, chronic catarrh, ascites, etc., constitute the principal agencies in the production of disorders of nutrition, which in all cases of cirrhosis sooner or later supervene in the second stage of the disease. First of all, a change in the color of the *skin* usually becomes visible; this part appears not merely anæmic, but acquires a dirt-colored tinge, or, together with the conjunctiva, a dirty pale-yellow look. Whether the latter is to be considered as a slight trace of icterus, or referred to products of the hæmoglobin otherwise produced, can hardly be determined when the urine does not respond to the reaction of bile-pigment,

because a quite similar discoloration occurs in cachexia from other causes. Subsequently the skin becomes flabby, dry, and desquamating. The wasting of the adipose tissue and the muscles begins usually at an early period, but advances now and then at the outset but slowly, in consequence of which a considerable corpulence may exist even after the volume of the liver has become preternaturally small; ultimately, however, extreme *emaciation* supervenes, which, contrasted with the swollen abdomen, appears particularly striking in the upper portion of the body.

As a rule, the affection is not of itself attended with *fever;* the febrile exacerbations of the chronic inflammatory process, which now and then appear in its early stage, have been already (p. 185) described. When, at other times, fever is occasionally present, this proceeds from acute exacerbations of the perihepatitis or of the catarrh of the digestive organs, or from complications.

The *urine* increases in quantity with the development of the ascites, and is then usually reddish-yellow or red, of a somewhat diminished specific gravity, giving very often precipitates of urates rich in pigment. The quantity of urea was found by Redenbacher nearly normal, that of the chlorides diminished. After the puncture of the abdomen the renal secretion is wont to increase during the three to four days following; on the other hand, it may sink to the minimum if a copious discharge is maintained from the opening made by the puncture. The diminution of the quantity of the urine in the second stage of interstitial hepatitis is attributable to a reduction of the pressure in the aortal system, which originates partly in the retention of a considerable quantity of blood in the portal system, partly in the escape of a large quantity of serum into the peritoneal sac, partly in the impediment presented to the lesser circulation in consequence of a narrowing of the thoracic cavity from distention of the abdomen.

Hematuria vesicalis was observed by B. Langenbeck[1] in hepatic cirrhosis, the idea of their mutual relation being based upon the fact that the liver by its increas-

[1] Archiv f. klin. Chirurgie. Bd. 1, S. 41.

ing degeneration may exert pressure upon the *cava inferior*, in consequence of which obstruction of the blood in the pelvic branches of the latter must supervene, and hemorrhage from the *venæ minoris resistantiæ*. In one of the cases, however, reported by the above-mentioned author it was not the sclerotic liver itself, but a firm, fibrous mass, composed apparently of morbidly changed lymphatic glands adherent to the concave surface of the organ and to the omentum, which compressed the *vena cava inferior;* and in the other case the hepatic disease was still in so early a stage that recovery followed a course of treatment at Carlsbad. Consequently the theory of hemorrhage from the bladder is not yet satisfactorily demonstrated to be a symptom—even quite rare—of cirrhosis.

The *respiration* is usually embarrassed in the later stage by the distention of the abdomen, the peritoneal transudation and the inflated intestine tending to force powerfully upward the diaphragm, and interfere with its contractility. Now and then, also, hydrothorax contributes to the dyspnœa.

As the anæmia increases the *pulse* becomes smaller, and at length also more rapid. Collapse not unfrequently ultimately ensues. In other respects nothing abnormal appears, as a rule, in the circulatory organs, except in cases where, in consequence of severe icterus or fever, the well-known changes in the heart's action and the tension of the arteries are induced.

E. Wagner, who found slight hypertrophy of the left ventricle in two cases in men thirty-three and thirty-six years old, one of whom, at least, had always led a temperate life (loc. cit., p. 474), has enunciated the hypothesis that between this lesion and the hepatic cirrhosis there exists the same relation as (according to Traube's theory) between the same cardiac affection and the atrophied kidney. I am not aware that the statements of any other observers would serve to confirm this idea. Where under other circumstances hypertrophy of the left ventricle has been noticed on post-mortem examination, there existed, in addition, either granular atrophy of the kidneys, or arterial sclerosis, or a valvular lesion in the left side of the heart. It appears to me, moreover, that the new formation of numerous vessels in relation with the ramifications of the hepatic artery, and situated in the interstitial tissue of the cirrhotic liver, does not speak in favor of this questionable hypothesis.

In the later stage of the disease, moreover, in those parts of the body where no impediment to the circulation from stasis of the portal blood can concurrently operate, capillary hemorrhages not unfrequently occur. Petechiæ and ecchymosis of the skin, and hemorrhages from the mucous membrane of the mouth and

nose, are the most frequent;[1] there, nevertheless, occur also extravasations in the intermuscular connective tissue, hemorrhages from the lungs, hemorrhagic transudations in the pleura, etc.[2] The immediate cause of these hemorrhages, or of what has been termed, by way of explanation, the *hemorrhagic diathesis*, is as yet unknown, although the very great impairment of the hepatic functions and the debilitated physical condition point probably to an abnormal condition of the blood and nutritive disorders in the intestinal wall.

As regards the *nervous system*, generally no symptoms are present. Even the spirits of the patient are less frequently depressed than in other chronic disorders of the liver.

Severe cerebral symptoms, such as somnolence, delirium, convulsions, coma, appear in many cases toward the end of life; and, indeed, not exclusively in such as are attended with icterus. The autopsy reveals then only exceptionally acute yellow atrophy of the granulations; far more frequently we are unable to demonstrate in the surviving glandular parenchyma any destruction of the hepatic cells. This justifies the theory that in cirrhosis, when this affection does not terminate fatally at an earlier stage as the result of complications, or of changes which it of itself induces in numerous other organs, the gradually progressing atrophy of the glandular parenchyma gives rise ultimately to precisely similar disorders of the brain as does acute atrophy of the liver.

Complications.

Among the manifold affections with which cirrhosis of the liver may be *complicated*, particular mention should, first of all, be made of those proceeding from the same cause, as well as those which have their seat in the same organ, on account of the

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[1] *Bruzelius* (Hygiea, 1873, S. 41; Virchow-Hirsch Jahresber. f. 1873, Bd. 2, S. 164) observed, in addition to repeated epistaxis, a considerable arterial hemorrhage from a teleangiectasis of the skin at the root of the nose.

[2] Hemorrhages in the retina of both eyes were observed by *Stricker* in one case, where the autopsy revealed also extravasations in the *dura* and *pia mater* above the convexity of the cerebral hemispheres.

influence exerted by them in shaping the general features and course of the disease.

To the former category belong probably the chronic changes of the *kidneys*, which are quite frequently encountered in connection with cirrhosis. These consist principally in granular and fatty degeneration of the epithelium of the cortical substance; although the processes characterized by the proliferation of interstitial tissue are not of very rare occurrence.

Liebermeister (loc. cit., p. 70) gives a description of the histological appearances found in a case of the latter class. In thirty-one autopsies, the results of which are communicated in abstract by G. Foerster from the records of the Berlin Pathologico-Anatomical Institute, nephritis is recorded three times, granular atrophy four times, and induration of the kidneys the same number. E. Wagner found among twelve cases, of which ten were habitual brandy-drinkers, eleven with "chronic nephritis."

Inasmuch as those pernicious influences, which are recognized with the greatest degree of certainty as causes of hepatic cirrhosis (chronic abuse of alcoholic spirits, malaria, syphilis), play their part also in the etiology of the diffuse affections of the kidneys, we not unnaturally conjecture, where hepatic and renal affections are coexistent, that there exists a causative factor common to both. The complication in question usually renders its presence known by albuminuria and general dropsy diffused over the upper portion of the body.

The parenchymatous degeneration of the *muscular tissue of the heart*, which is frequently found in the bodies of cirrhotic patients, may generally be regarded, at least in drunkards, as a result of the abuse of spirituous liquors. At other times it is an accidental complication due to advanced age. In individual cases it is attributable to a very extensive impairment of the nutritive functions, otherwise manifested by fatty degeneration of the hepatic cells and the epithelial of the kidneys. Where the degeneration of the cardiac musculature is developed in more chronic form, it tends to induce dropsy and the approach of collapse.

Affections of the *brain* and its *membranes*, being peculiar to chronic alcoholism, are also occasionally met with in cirrhotic

patients. E. Wagner found among nine patients as many as five cases of chronic pachymeningitis, partly in the form of decided thickening and attachment of the *dura mater*, partly as new-growth of vascular connective tissue on its inner surface with consecutive hemorrhages. However, these complications often remain latent during life.

Among the affections occurring in the liver itself simultaneously with cirrhosis, amyloid degeneration and fatty infiltration, as well as the influence of both these lesions upon the size of the organ, have been already referred to. Thrombosis of the portal vein, which is an occasional adjunct of cirrhosis, promotes the development of the symptoms arising from obstruction, and accelerates the re-formation of the ascites after puncture. Cholelithiasis, as was long since observed by Budd,[1] appears to occur comparatively seldom in this connection. Combinations with cancer of the liver and of the portal vein are occasionally seen; in cases of this class the peritoneal transudation is frequently of a highly hemorrhagic character.[2] Complications with hepatic abscess are reported by Bamberger; those with echinococcus by G. Foerster.

From among the remaining diseases which are met with in certain cases in conjunction with cirrhosis, allusion should be made to cardiac affections and pulmonary emphysema, which tend to promote the development of symptoms arising from obstruction, and impart a general character to the dropsy. In view of their rarity, complications with leucæmia deserve mention.[3] Those with diabetes mellitus appear to be still more rare; this variety occurred in one case reported by Budd (loc. cit., p. 148); moreover, Leudet (loc. cit., p. 560) observed in one instance during the first stage of interstitial hepatitis a slight glycosuria, with increased thirst.

Acute and, for the most part, inflammatory processes, a pre-

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[1] Die Krankheiten der Leber. Deutsch von Henoch. S. 315.

[2] Compare the observations of *Corazza*, Bull. delle scienze med. di Bologna, Ser. 5, Vol. 11, p. 342 (Virchow-Hirsch Jahresber. für 1871, Bd. 2, S. 164); and of *Fitz*, Boston Med. and Surg. Journal, May 2, 1872 (Virchow-Hirsch Jahresber. f. 1872, Bd. 2, S. 165).

[3] *Mosler*, Die Pathologie und Therapie der Leukämie. S. 85 und 259. *Leudet*, loc. cit., p. 56.

disposition to which is induced chiefly by cachexia, but in part also by certain local changes, frequently supervene in cirrhosis—such as, for instance, pneumonia, especially in topers; furthermore, bronchitis, pericarditis, general peritonitis,[1] intestinal diphtheria, erysipelas and gangrene of the œdematous skin.

Diagnosis.

In most cases the question of diagnosis arises at a stage when numerous symptoms are already present; of these, those which when coexistent render probable the presence of the disease are the following four: ascites, unaccompanied by œdema of the lower extremities or appearing previous to the latter lesion; enlargement of the spleen; diminution in size of the liver; cachexia. If, in addition, the existence of one of the more common etiological factors can be demonstrated, then the probability becomes very great. It does not amount to a certainty, however, strictly speaking, until we have succeeded in feeling the granulations. The diagnosis is often first of all rendered possible by puncture, not only from the circumstance that immediately after the evacuation of the peritoneal transudation the abdominal integument, then relaxed, permits, as a rule, the manipulation of the liver, but also because previous thereto we are often quite unable to define with certainty the size of the organ. Where we succeed in demonstrating only the diminished volume and increased consistence of the liver, but not the granulated condition of its outer surface, it must then remain undetermined, whether we have to deal with cirrhosis or that form of *chronic perihepatitis*—extremely rare, no doubt—in which, owing to the great shrinking of the thickened capsule, a diseased condition is developed completely analogous in other respects to that of cirrhosis. Moreover, two other diseases of the liver, which likewise occur far more rarely, indeed, than cirrhosis, are occasion-

[1] *Rokitansky* (Lehrbuch der pathol. Anatomie, Bd. 3, S. 259) describes "hemorrhagic-tubercular pseudo-membranes" in peritonitis, developed intercurrently with cirrhosis; moreover, among thirty-one reports of autopsies collected by *G. Foerster, peritonitis tuberculosa* is found recorded in three instances.

ally so similar to it in appearance that they can be distinguished only when we have an opportunity of tracing their course, or when the etiology furnishes a sufficient clue; these are occlusion of the portal vein by adhesive thrombi, or by compression, or by simple atrophy of the liver. The *occlusion of the portal vein* appears invariably as a secondary lesion consecutive upon other chronic diseases of the abdominal organs, and is usually followed by a more rapid development of the symptoms arising from mechanical obstruction than is cirrhosis; but, on the other hand, this lesion never gives rise to enlargement of the liver, nor, indeed, to such remarkable lessening in size, as frequently takes place in cirrhosis. In *simple atrophy*, which occurs almost exclusively in decrepit persons, and in which it is in exceptional instances only that ascites supervenes earlier than anasarca, the reduction in volume proceeds at a uniform rate in both lobes; in cirrhosis, on the other hand, it is, as a rule, quite far advanced in the left lobe, when in the right it first begins to be perceptible. *Diffuse chronic* peritonitis—the simple form as well as the tuberculous and cancerous variety—presents, moreover, under certain circumstances a complication of symptoms which render the diagnosis from hepatic cirrhosis extremely difficult. Where there exists an abundant exudation the fluctuation may be as evident and as extensive as in ascites, while the liver, being forced upward and backward, may be apparently diminished in size; here enlargement of the spleen may also be present (especially in tuberculosis, but also—according to Galvagni[1]—in simple peritonitis), while the sensitiveness of the abdomen is wanting. In cases of this class a careful consideration of the remaining conditions will occasionally aid us in forming a correct diagnosis: simple and tuberculous peritonitis are, as a rule, attended with fever, and the skin does not present that dirty yellowish hue observed in cirrhosis, but is simply pallid; in tuberculosis and cancer of the peritoneum there are commonly found, too, in other organs, changes important as regards the diagnosis (caseous deposits in the epididymides and lymphatic

[1] Rivista clin. di Bologna. 1869. Virchow-Hirsch Jahresbericht pro 1869. Bd. 2, S. 158.

glands, carcinoma of the abdominal viscera and of the mamma). The *cyanotic atrophy and induration* of the liver is characterized, indeed, in common with genuine cirrhosis, by a gradual reduction in the volume which is usually at the outset enlarged, and by the presence of ascites; but the anasarca precedes here the ascites, and the dependence of the symptoms upon the insufficient action of the right ventricle may be determined with certainty from the appearances found in the circulatory and respiratory organs. A persistent *occlusion of the large excretory bile-ducts* (*ductus choledochus* or *hepaticus*), which ultimately gives rise, likewise, to a gradual reduction in the size of the liver, is distinguished—independently of the symptoms of the highest grade of biliary obstruction which may also be present in cirrhosis in consequence of complications—from the latter by the circumstance that it does not induce swelling of the spleen, and that ascites is either absent, or it falls far short of attaining that height usually met with in cirrhosis. In exceptional cases only is the diagnosis rendered difficult by the fact that, notwithstanding the appreciable diminution in the volume of the liver, the results of the mechanical obstruction of blood in the roots of the portal vein are but very slightly developed, or are altogether wanting, for the reason that a compensatory collateral channel has been established through vessels not accessible to observation—*e. g.*, the inferior œsophageal veins.

In the first stage of the disease, while the organ is still enlarged and its outer surface smooth, as regards *amyloid degeneration of the liver*—which, likewise, occurs in the train of syphilis and intermittent fever, and is, as a rule, accompanied by amyloid enlargement of the spleen—the circumstance that this disorder is invariably attended by pronounced cachexia should be regarded as significant, whereas in cirrhosis such a condition is not wont to exist in the earlier part of its course; the subsequent diminution in volume of the liver will, however, often first of all decide the affair. It is almost always easy to avoid confounding the disorder with other affections in which the organ presents an increased volume; *cancer of the liver*, when forming no nodules that can be felt, may most readily give rise to such a mistake.

Course, Modes of Termination, Prognosis.

In consequence of the obscurity attending its origin, the *duration* of the morbid process cannot be accurately determined. The period intervening between the appearance of the first symptoms of the disease and death, varies in different cases within very wide limits. If we reckon from the symptoms of the hepatic hyperæmia, which appears often to accompany the beginning of the proliferation of the interstitial tissue, there are then cases in which the disease lasts three years and longer. Others again are seen to terminate under the influence of complications where a period of weeks only has elapsed since the cirrhosis first became noticeable. According to an observation reported by Stricker from Traube's clinique, the course may, however, be quite rapid even where no complications exist: in the case in question, relating to a man thirty-six years old and addicted to the moderate use of liquor, only six weeks intervened between the initiatory symptoms of the disease and death.

In cases that have been accurately diagnosticated the *termination* is, without exception, death. Although the derangements which are, as a rule, induced by the obstruction of the portal circulation are here and there diminished, and possibly even compensated for by the dilatation of collateral channels, still the continuously progressive reduction in volume of the secreting parenchyma becomes ultimately in itself a source of danger. There admits, indeed, of no doubt that the injurious effects of the disappearance of numerous hepatic cells may be limited and postponed by the enlargement or multiplication of those remaining ; but the cases of cirrhosis, in which hypertrophy or hyperplasia of the hepatic cells has as yet been observed, were not at the same time those in which compensation for the circulatory disturbances had occurred. Another question is, whether healing may result in such a manner that an arrest of the process takes place in an earlier stage of development, when sufficient capillaries and hepatic cells have not as yet been destroyed as to occasion thereby any appreciable disturbances. But even this possibility is thus far unsupported by proof. For although

cirrhosis not far advanced has been occasionally observed on post-mortem examination of individuals who have died from other diseases without having presented during life any symptom of hepatic affection, we surely should not be justified in drawing thence the conclusion that there exists a milder, non-fatal form of the disease; for cirrhosis, even in a majority of the cases in which it ultimately produces death, continues for a comparatively long time without symptoms.

It often happens that death does not result until the marasmus has attained the highest degree; frequent diarrhœa and complete anorexia tend to induce exhaustion; there finally supervenes pulmonary œdema, or collapse protracted frequently through many days. In exceptional cases life is suddenly extinguished unexpectedly by profuse vomiting of blood. Not unfrequently it is acute and for the most part inflammatory processes—such as pneumonia, pleuritis, peritonitis, and others mentioned above under complications—which, by their supervention, tend to hasten the end. Death is frequently ushered in by the same cerebral symptoms as are observed in acute atrophy of the liver.

The *prognosis*, when no doubt exists as to the nature of the disease, is absolutely unfavorable. How long life may still linger in special cases can only be conjectured from an estimate of the amount of physical strength still present, the condition of the digestive organs, casual complications, and the external relations of the patient. Individual patients are seen to survive the appearance of ascites under judicious nursing, care, and treatment for a year, and even longer. According to an observation of Leudet (loc. cit., p. 456) the ascites may disappear even for a period of several years, and during this interval convalescence may, apparently at least, continue; it seems to me, however, that the case in question should not be included at all under the head of cirrhosis.

The case relates to a spirit-drinker, sixty years old, in whom, in 1857, after long-persistent gastric disorder, ascites was developed. Puncture, by means of which twenty litres were evacuated, was followed by gradual improvement; the patient was enabled to resume work, and continued tolerably well for a period of three years. In June, 1860, considerable ascites was developed anew, and the puncture,

which very soon became necessary, as well as a second undertaken fourteen days afterward, gave escape to a sanguinolent fluid. In consequence of a hemorrhage from the bowels, death ensued at the end of July, 1860. On post-mortem examination there were found in the abdomen some old false membranes and sanguinolent fluid; the liver was enlarged by one-third, and studded with distinct cirrhotic granulations; its cells were infiltrated with a finely granular, fatty mass, and the connective tissue somewhat hypertrophied (*un peu d'hypergenèse de la trame celluleuse*); the spleen was enlarged to double the natural size; the trunk of the portal vein was plugged by a whitish, adherent coagulum. Here the first effusion into the peritoneal sac was the result, in all probability, of a simple chronic peritonitis; whereas that occurring three years later, as well as the hemorrhage from the intestines, was produced by the thrombosis of the portal vein, which formation had arisen, presumably, in the shrivelling peritonitic new-growths in the *porta hepatica*.

Treatment.

In spirit-drinkers, or in individuals with respect to whom the existence of some one of the other etiological agencies justifies the assumption that they are in danger of becoming affected with cirrhosis, a *prophylactic* treatment is indicated as soon as signs of hepatic hyperæmia or perihepatitis make their appearance. Then all alcoholic liquors, irritant spices, strong coffee, and similar articles are to be prohibited. In robust individuals the amount of meat consumed should be limited, and the nourishment should consist chiefly of a milk and farinaceous diet, simple vegetables, and fruit. If the pain is violent, then quiet rest in bed is requisite, and venesection beneath the right arch of the ribs, and in the vicinity of the anus, followed by moist, warm applications to the region of the liver; internally mild saline purgatives, bitter-waters, and the like. Where there exists dull, long-persistent pain, then a course of Carlsbad, Marienbad, or Tarasp waters is indicated, or, in less vigorous persons, the springs of Franzensbad, Elster, or Kissingen. Moreover, after the above-mentioned symptoms have been allayed, it is advisable that such symptoms as point to chronic hepatic hyperæmia should, for a still longer period, be kept under observation. Malarial patients should be treated in the manner detailed in Volume II. of this Cyclopædia, p. 655, and should be transferred, if possible, to a more healthy locality. Where we can assume syphilis to be the cause, then the treatment appropriate to this

indicatio causalis must be adopted. In all other cases the internal and external use of preparations of iodine and mercury are of extremely doubtful utility; yet English practitioners prefer to administer, even at this late day,[1] mercurial purgatives.

The late stage of the affection, which most cases have attained when they apply for medical advice, almost invariably[2] permits only a *symptomatic* treatment. Violent measures and debilitating remedies are then, above all, contraindicated; their application would only tend to accelerate the unfavorable termination. In case of any casual exacerbation of the perihepatitis, we should therefore avoid, if possible, blood-letting, or, at the most —provided quiet rest with warm, moist applications be not sufficient—a few cupping-glasses should be applied. The most important indication at this time is to keep the nutrition of the patient as long as possible up to a fair standard, or, where this has already sunk to a low point, to restore it. To attain this result several methods must usually be resorted to. First of all, the condition of the stomach and the intestines requires attention: in order to combat the chronic catarrh of these organs, the carbonated alkalis, either alone or in combination with a slight quantity of aromatic or bitter remedies, small doses of Carlsbad salts, preparations of rhubarb and aloes in eccoprotic doses, and the like, are most frequently appropriate. Frerichs recommends, for regulating the digestive functions of the intestine and for allaying the tympanites, choleate of soda dissolved in an infusion of rhubarb or in some aromatic water. We should then prescribe a nutritious diet, the most suitable to the condition of the digestive organs, and, in case of patients very much reduced, the indulgence in a moderate quantity of wine or beer. Finally, the use of preparations of iron proves often of benefit; from these should be selected those which do not disturb the patient's stomach. The diminution of the ascites which is now and then seen to ensue in neglected cases, attributable solely to the influence of improved diet and the administration of iron, indicates

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[1] Compare *Habershon*, Guy's Hosp. Rep. 3. Ser. XVI. 1871, p. 319.

[2] With reference to the cases produced by syphilis, *vide* chapter on Syphilitic Hepatitis.

plainly the part played by anæmia in the transudation from the over-distended peritoneal vessels.

In other respects, any pharmaceutical treatment directed toward the ascites is seldom followed by any result. Where the affection has originated in a malarial infection, quinine seems to prove of decided benefit. Diego Coco[1] relates a case of this class where, after the continued administration of quinine, reinforced by a number of cold douches, the ascites abated completely, and the patient was discharged with liver reduced in volume and, "upon the whole, almost cured" six months after his entrance. The ordinary *diuretics* prove, in exceptional instances only, efficacious, and even then it is, in all probability, when the development of the ascites is promoted by a derangement of the renal secretion, which, originating in some complication of the cirrhosis, is amenable to the action of this or that diuretic. At all events, observations like the following, by C. Handfield Jones,[2] would scarcely be explicable otherwise than in this manner.

In an old toper, thirty-four years old, suffering from considerable ascites, splenic enlargement and severe hemorrhages from the stomach and bowels, after the second puncture, which, as well as the first, had evacuated ten pints, there ensued, under the use of digitalis, copious diuresis, as the result of which the circumference of the abdomen was reduced from 39½ to 33½ inches.

On the other hand, another agent, not used as a diuretic in Germany, has proved, according to the experience of English physicians, of decided benefit. This is the balsam of copaiva. Garrod, Duffin,[3] Sieveking,[4] Wilks,[5] observed after the use of balsam of copaiva, administered three times daily, in doses of from ten to twenty grains (0.6–1.3)—or what, according to Wilks, is probably still more efficacious, the resin of copaiva—the quantity of urine increase two- or four-fold, while the dropsy disappeared.[6] Quite as brilliant a result was obtained, moreover, in

[1] Il Morgagni Disp. VII., p. 469.

[2] British Medical Journal. 1871, March 4.

[3] The Lancet. 1869, Feb. 27.

[4] Ibidem. 1870, Dec. 17.

[5] Ibidem. 1873, March 22.

[6] Compare *Brudi*, Deutsches Archiv f. klin Med., Bd. XIX. (1877), S. 511 ff., where will be found reported, in addition to two other cases quoted from the English

a case reported twenty years ago by Klinger (loc. cit., p. 554), by the administration of the ethereal spirits of turpentine, in doses of twelve drops twice daily. The *drastic cathartics* have also been frequently employed to reduce the ascites. These agents may, indeed, have the power of lessening the pressure in the portal vein, and thereby inducing a resorption of the fluid from the peritoneal sac; but, in all probability, they produce this effect solely by stimulating the peristaltic action, and thus checking the resorption of the liquid contents of the intestine (Radziejewski); whereas their action tends also to derange the digestive functions of the bowels, while the appetite disappears, and vomiting readily ensues; in many cases, too, even after the drastic agents have been suspended, the diarrhœa does not cease. The exhibition of medicaments of this class tends to accelerate, therefore, in patients already debilitated the approach of collapse, and even in patients who are still robust it produces, as a rule, by its pernicious action upon the digestive organs, an injury relatively greater than the benefit accruing from the diminution of the ascites. In quite exceptional instances it undoubtedly seems to have a strikingly favorable effect: thus, an observation is reported by Leudet[1] of the case of a wine-dealer, fifty-three years old, whom it had been necessary to puncture three times within a little less than five weeks; beginning with the tenth day after the last puncture, inasmuch as the ascites had already again attained to a considerable quantity, gamboge was administered for six weeks in large doses (from seven to fifteen grains daily; in all, five drachms): the ascites diminished materially with the watery stools, and during the subsequent two years had disappeared completely, notwithstanding the very great emacia-

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literature of the subject (*Thompson*, Transact. of the Clinical Society of London, Vol. III., p. 26; and *Liveing*, ibid., p. 30), also a case observed in Freiburg by *Dr. Thiry*, where, in a case of cirrhosis hepatica alcoholica with enormous ascites, a prompt diuretic action of the resin of copaiba was likewise noticed. The remedy was here administered according to the following formula: ℞. *Resinæ copaibæ*, ℥iv.; *sodii carbonatis*, ʒ ss. *Misce; fiant pilulæ* No. 50. S. "Five pills three times daily." In three cases of severe cirrhosis in which I have given this remedy, it failed to have any influence upon the diuresis.

[1] Loc. cit., p. 547. Obs. XIII.

tion of the patient. But, even apart from the circumstance that in this case there was no verification of the diagnosis by post-mortem examination, it will pass, nevertheless, at most as an extremely rare exception, and cannot overthrow the principle derived from experience, that the better procedure is, to abstain altogether from the administration of drastics in cirrhosis. It results, therefore, that in the operation of paracentesis we possess the means of lessening with greater certainty and promptness serous accumulations within the abdominal cavity, the judicious use of which is not commonly attended with any direct danger. The wound thereby inflicted gives rise relatively quite seldom to erysipelas of the abdominal integument or to peritonitis. The functions of the stomach and intestinal canal are even wont to be improved after puncture; while, with the removal of the pressure previously exerted by the mass of ascitic fluid and by the tension of the distended abdominal integument upon the vessels of the intestinal *serosa*, there results a decided filling-up of the latter, accompanied by a diminution of the venous hyperæmia in the remaining coats of the intestinal wall. But there again ensues also from the more completely filled peritoneal vessels, when the obstruction to the hepatic circulation continues, a more copious transudation and an increased loss on the part of the blood of its plasma[1] rich in albumen. This offers an explanation why tapping affords invariably but transitory amelioration, and why, notwithstanding the improvement which in many respects is thereby induced, it cannot arrest the progress of the general impairment of the nutritive functions. This operation, therefore, must not be undertaken unnecessarily, but only in response to an urgent indication. Such an indication is offered where the dyspnœa arising from upward displacement of the diaphragm threatens life, or where an obstinate vomiting is probably attributable to mechanical derangement of the digestive canal due to the large amount of ascites. If under these circumstances alone we resort to paracentesis, it will accomplish

[1] The attempt to prevent the reaccumulation of the ascites by the stimulation of adhesive peritonitis by means of iodine injections into the abdominal cavity, is quite as useless as it is dangerous, as would be *à priori* imagined, and as is proved by the experience of *Strohl* (Gaz. de Strasb. 1855. Nr. 5).

all that can be expected from any symptomatic treatment. This is most clearly demonstrated by the fact that cases are not rare where an opportunity has been afforded of repeating[1] the operation several or even many times.

The other serious and dangerous symptoms, and the complicating affections which may supervene in the course of cirrhosis, we should attempt to combat—while bearing constantly in mind the physical condition of the patient—with such remedies as are suggested by the treatment directed toward the primary changes in the organs in question.

II. Rarer Forms of Interstitial Hepatitis.

Gluge, Atlas d. pathol. Anat. Lief. 2, S. 4. Taf. 1.—*Frerichs*, Klinik. Bd. 2, S. 90 f.—*Henoch*, Klinik der Unterleibskh. 3. Aufl., S. 83.—*Liebermeister*, Beiträge. S. 135 f. und S. 144 f.—*Jaccoud*, Gaz. des Hôp. 1867. Nr. 69, 71, 72.—*H. Mollière*, Jour. de Méd. de Lyon, 1868; Gaz. hebdom. de Méd. et de Chir., Ser. 2, Vol. 5, p. 765.—*P. Ollivier*, Union médic. 1871. Nr. 68, 71, 75.—*Leudet*, Clin. médic., p. 48 sqq.—*G. Hayem*, Arch. de physiol. norm. et pathol. 1874, p. 126 sqq.—*Cornil*, Ibid., p. 265 sqq.—*C. Hanot*, Étude sur une forme de cirrhose hypertrophique du foie. Thèse de Paris, 1876.—*Charcot* et *Gombault*, Arch. de physiol. 1876, p. 272 sqq. u. p. 453 sqq.—*Du Castel*, Arch. génér. 1876. Vol. II., p. 264 sqq.—*v. Fragstein*, Berl. klin. Wochenschr. 1877. Nr. 16, 17, 19.

While in ordinary cirrhosis the parenchyma-islets, separated from each other by the streaks of indurated tissue, consist usually of larger or smaller *groups of lobules*, in the variety of interstitial hepatitis now under consideration, the proliferation of connective tissue takes place between the *individual lobules*. This difference has been most distinctly pointed out by Charcot and Gombault. By these writers ordinary cirrhosis

[1] *Leudet* (loc. cit., p. 557) recommends, in cases where the umbilicus is distended in the form of a sac, that paracentesis should be made at that point by means of a fine (explorative) trocar. In a man fifty-seven years old, in whom great exhaustion followed the first two punctures made with an ordinary trocar, no unfavorable effect, either at the seat of the operation or in the general condition of the patient, was manifested after capillary puncture, which was undertaken fifteen times within thirteen months, producing each time within from three and one-half to four and one-half hours an almost complete evacuation of the transudation.

is designated *annular* or *multilobular*, because in this form a great many lobules are encircled by a fibrous ring; this they distinguish from *insular* or *monolobular* cirrhosis, in which the new-growth assumes, first of all, the form of small islets in the interlobular spaces, then invests more or less completely each lobule, and finally penetrates beneath the rows of hepatic cells, which are thereby forced apart, and, without presenting any other changes, are ultimately destroyed by simple atrophy. Inasmuch as the parenchyma-islets in the fibrous tissue are here, for the most part, formed from the individual lobules, they are much smaller and less sharply defined, but they are more uniformly distributed than in ordinary cirrhosis. As compared with the latter, the proliferation is commonly more extensive, and may continue longer; the shrinking, on the other hand, ensues later and more slowly.

The change described especially by German authors (Henoch, Frerichs, and others) merely as *induration*, or *simple induration of the liver*, depends upon interstitial hepatitis of the monolobular type, as is demonstrated by an histological appearance detected by Liebermeister (loc. cit., p. 146) in a case of this sort.

By this name is usually designated merely the last stage, yet the term has of late been also employed with reference to the process while yet undergoing development. Compare A. Thierfelder, Pathol. Histol., T. 14, Fig. 3; and Birch-Hirschfeld, Lehrb. d. pathol. Anat., Lpz., 1866, S. 939.

When the simple induration is completely developed, there is substituted in the place of the hepatic parenchyma a dense mass of connective tissue, in which every trace of the glandular structure has disappeared; or, at the most, the remnants of the hepatic cells are still indicated by brown, uniformly distributed dots. It will be understood that, in its extreme grade, the change never implicates the entire organ; generally the homogeneous fibrous mass penetrates from the surface more or less deeply into the parenchyma; in the left lobe it sometimes extends through its entire thickness. The bile-ducts, and usually the ramifications of the portal vein implicated in the indurated parts, are dilated. The other parts either present the characteristics of granular induration, or are perfectly normal. Where the uniformly dense mass

involves the greater part of the organ (as, *e. g.*, in Gluge's case three-fourths, in that of Henoch three-fifths), the volume and weight may be very much increased (in Gluge's case the liver weighed five and three-quarter pounds). The outer surface is sometimes smooth, and sometimes exhibits larger or smaller eminences, which resemble in size and shape those of the coarsely granular liver, but consist altogether, or in the main, of indurated tissue.

The causes appear to be the same as in ordinary cirrhosis; in the case observed by Frerichs the affection was developed once after intemperance, once after intermittent fever, and twice as a supplement to chronic peritonitis. (With respect to its origin from chronic inflammation of the gall-ducts, *vide* following chapter.) Moreover, the symptoms correspond essentially with those of ordinary cirrhosis, except that the sensitiveness of the hepatic region was found by Frerichs to be greater and more extensive in simple induration; and, according to the observations of Gluge and Henoch, in addition to ascites and copious hemorrhages from the digestive tract, considerable enlargement of the liver may also be present and continue until death. It is impossible during life to distinguish this from other forms of interstitial hepatitis, while the treatment, too, presents no other indications than those found in ordinary cirrhosis.

Interstitial Hepatitis arising from Affections of the Gall-ducts.

During the *formation of gall-stones within the liver* there may proceed from the walls of the gall-ducts that are filled with concretions a proliferation of connective tissue, which gives rise in the immediate vicinity of the affected portion of these canals to induration of the hepatic parenchyma, but which may also extend, in exceptional cases—as has been shown by Liebermeister (loc. cit.) in a case very accurately described—to the interlobular structure of the entire gland, inducing a condition that corresponds in all essential histological respects to cirrhosis.

A further instance of this mode of development of the affection is apparently presented in an observation reported as long ago as 1857, by Berlin (Nederl.

Tydschr. I., p. 231; Schmidt's Jahrb., Bd. 99, S. 43): here even the clinical appearances of cirrhosis were not wanting; the induration (which Berlin, following the example of Schroeder v. d. Kolk, designates *albescentia hepatis*) was limited, however, to the left lobe and the adjacent portion of the right; the gall-ducts in these portions of the organ contained partly gall-stones and in part inspissated bile.

That *morbid conditions of the ductus choledochus* associated with long persistent biliary obstruction may result in interstitial hepatitis, is a theory advocated with more or less positiveness by different authors during the latter decades.

As long ago as 1857, in the discussion of a case where the discharge of gall was in repeated instances for a long period obstructed by gall-stones, and where on post-mortem examination the liver was found to be slightly granular and its interstitial tissue moderately increased, it was clearly shown by Virchow (Verhandl. d. phys.-med. Ges. zu Würzb., Bd. 7, S. 27) that this condition of the liver might very possibly be regarded as a result of the irritation due to the presence of gall-stones. B. Cohn (Guensburg's Zeitschr., Bd. 5, H. 6), in 1864, described as a special form of cirrhosis the icteric, in which, in consequence of prolonged pressure upon the sides of the over-distended gall-ducts, obliteration of the interlobular blood-vessels and proliferation of connective tissue in their neighborhood may take place, the liver being thereby reduced to a state of granular atrophy; but no confirmatory observation was communicated by him. Next (1866), O. Wyss (Virch. Arch., Bd. 35, S. 559) asserted that in long-persistent icterus of the liver he had frequently found the interlobular connective tissue more or less, though never very greatly, increased. Experiments instituted by H. Mayer (Wien. medic. Jahrb., 1872, II., S. 133), and by Wickham Legg (St. Bartholomew's Hosp. Rep., Vol. IX., p. 161), on cats, and by Charcot and Gombault on guinea-pigs, uniformly proved that in these animals the ligature of the *ductus choledochus* induces an active proliferation of connective tissue, not only between the lobules, but also within them; and consequently, if the animals live long enough, the entire organ undergoes no slight increase in volume and consistence. According to an Observation of Legg, there may apparently result a diminution in the volume and granulation. Charcot and Gombault found, moreover, in the periphery of the lobules extremely numerous fine gall-ducts joined together in the form of a net-work (according to their view, dilated bile-capillaries, which have preserved an epithelial coating). The investigators last named have also demonstrated in the cases of two men where the *ductus choledochus* was occluded (once by a gall-stone, the other time by a cancer of the head of the pancreas) such an extra- and intra-lobular new-formation of connective tissue with consecutive diminution of the lobules (in consequence of simple atrophy of the hepatic cells) and an increase of the interlobular gall-ducts, very slight, indeed, compared with that observed in the animals experimented upon.

The interstitial hepatitis induced by narrowing or occlusion of the *ductus choledochus* is as yet of interest mainly from a pathogenetic and pathologico-histological point of view. Whether it can attain a degree in which the changes attributable to it will lend also expression to the clinical features, cannot be ascertained with certainty from the observations thus far made.

In both the cases examined by Charcot and Gombault the process was still in a very early stage. With respect to one, the histological appearances only are reported; in the other the patient presented no symptoms from which the existence of interstitial hepatitis could be inferred. Three further observations, which have been communicated by L. S. Beale, Du Castel, and v. Fragstein as examples of cirrhosis induced by closure of the *ductus choledochus*, would be very well adapted to illustrate the clinical importance of this lesion, if they did not seem open to question, partly in an etiological, partly in a symptomatological respect. The case of Beale (Archives of Medicine, Vol. I., p. 125), my knowledge of which is derived solely from the abstract given by Charcot and Gombault, is that of a man, forty years of age, in whom there had existed for a period of two years symptoms of hepatic disease—icterus, and finally ascites, rendering necessary the operation of paracentesis. On post-mortem examination there was found at the point of junction of the *ductus cysticus* and *hepaticus* a firm tumor, composed of lymphatic glands, by the pressure of which the discharge of bile was almost completely obstructed, and a somewhat enlarged, firm, and pale liver, with uneven outer surface, in which the newly-formed fibrous tissue encircled the separate lobules. Here there are, surely, grounds for suspicion that an inflammation of the connective tissue on the one hand, and the swelling of the lymphatic glands on the other, by their extension to Glisson's capsule, may have occasioned also the cirrhosis. In the case of Du Castel, where the *ductus choledochus* just anterior to its duodenal orifice contained a calculus, along the side of which, however, bile could still flow, the liver, being perceptibly enlarged and smooth on its surface, exhibited a general dilatation of the gall-ducts, and the histological characters of monolobular cirrhosis; but the patient is described as a "moderate drinker," and the icterus did not appear until other disorders, connected, in all probability, with interstitial hepatitis, had already existed for the period of a month. The patient of v. Fragstein had experienced, about twelve years previously, during the course of an affection associated with gastric colic, anorexia and vomiting, an attack of icterus lasting three months; during the last half year of her life she suffered from cardialgic and dyspeptic complaints, became more and more emaciated, and acquired four weeks previous to death dropsy, beginning in face and feet, which soon became general. The autopsy disclosed a liver somewhat reduced in size and flabby, with roundish protuberances on the surface not larger than a small hazel-nut, and a lobulated appearance at the brownish-yellow (not icteric) cut surface; the *ductus choledochus* was greatly dilated (more than two centimetres in circumference) at its orifice, as well

as throughout its whole course; the gall-bladder was thickened and shrivelled, and the *ductus cysticus* obliterated; the spleen was enlarged to double and moderately firm; the mucous membrane of the stomach extremely vascular, and its vessels tortuous; the kidneys swollen. Microscopically, the interlobular gall-ducts presented quite thickened walls, and were invested with broad, concentric layers of fibrous tissue; the extra- and intra-lobular connective tissue was considerably increased, for the most part thick and tense, but here and there studded more or less abundantly with lymphoid cells; the hepatic cells partly diminished in size, the peripheral filled chiefly with fat, the central with pigment; also biliary concretions in the bile-capillaries; the lobules at certain points either entirely disappeared, or reduced to scanty remnants; in the kidneys the epithelium of the convoluted tubes swollen, and exhibiting granular cloudiness in varied degree; in the straight tubes intact and shrunken blood-corpuscles and isolated fibrinous casts. V. Fragstein concludes from the changes found both in the large and finest biliary ducts that there had previously existed a biliary obstruction, and refers its cause to a chololithiasis which had given rise at the time of the icterus, lasting three months, to obstruction of the *ductus choledochus;* the cirrhosis is regarded by him as the result of this biliary obstruction, and the fine cellular infiltration—in part still abundant—of the interstitial connective tissue he considers as proof that the process continued to progress until the last. If this view is correct, the interstitial hepatitis appears in this case to have been by no means intense; for, notwithstanding that it lasted twelve years, it had not induced any decided induration of the liver ("the entire organ was flabby"), and, apart from the tortuous course of the gastric vessels, all proof of stagnation in the portal system was wanting. It appears, therefore, very questionable whether we are justified in attributing (as v. Fragstein has done) the severe digestive disorders, and indirectly also the degeneration of the kidneys, to the hepatic disease.

Konr. Lotze, in the recent report of a case of granular induration of the liver of high grade associated with congenital defect of the excretory bile-ducts (Berl. klin. Woch., 1876, No. 30), has suggested the possibility that this defect is to be considered as resulting from an imperfect development, and that the bile, thereby prevented from flowing off, may constitute a source of inflammatory irritation to the connective tissue of the liver. Yet, the circumstance that the newly-formed fibrous tissue was especially hard and tense just at the lower surface of the organ and around the ramifications of the portal vein, would tend to favor the ordinary theory, according to which a fœtal perihepatitis forms the primary lesion in these cases, which, by its extension to Glisson's capsule, gives rise to obliteration of the gall-ducts and also to hyperplasia of the interlobular structure.

Hypertrophic Cirrhosis, Hypertrophic or General Sclerosis of the Liver.

The form of interstitial hepatitis, recently described under the above name by French writers (P. Olivier, Hayem, Charcot, and Gombault), is distinguished pathognomonically by the circumstance that the diminution in the volume of the organ, resulting from the shrivelling of the newly-formed connective tissue, such as characterizes the later stage of ordinary cirrhosis, does not supervene, not even where the process continues for a long while, but the hyperplasia preponderates even until the fatal termination of the affection.

Among the observations which have been published as examples of this form of the disease, and, likewise, as proofs of its existence, there will be found comparatively many in which at the very commencement, or at least at a very early stage, decided icterus makes its appearance, not usually associated, however, with decoloration of the fæces, and persists—though with fluctuations—during the entire subsequent course of the affection. The cause of this phenomenon is attributed by the French investigators (Cornil, Hanot, Charcot, and Gombault) to changes in the small gall-passages. According to their observations, although no obstruction of the secretion nor inflammation can be demonstrated in the larger bile-ducts, the interlobular canals become dilated and ramify into finer ducts, forming immediately in front of the margin of the lobule a network, from which still finer branches proceed, to disappear between the hepatic cells. All these canals are lined with cubical epithelium; in the ultimate divisions the calibre often appears to be plugged with this epithelium. In the vicinity of these canals the indications of this new-formation of connective tissue are the most distinct. According to the views of the above-mentioned authors, the network of the finest gall-ducts lies already in the peripheral zone of the lobule, whose hepatic cells have here been compressed by the proliferating connective tissue, and reduced to atrophy; it is, consequently, none other than the network of bile-capillaries, which in some unexplained way have acquired an epithelial

lining. Hanot, as well as Charcot and Gombault, bases upon these appearances the theory, that in the cases of hypertrophic cirrhosis accompanied with early icterus, the primary lesion consists of an inflammation (spontaneous) of the interlobular gall-ducts induced by some unknown cause, and that the interstitial proliferation takes its start from the walls of these ducts. They, therefore, distinguish "*hypertrophic cirrhosis with icterus*" as a special form, and include it in the same group with interstitial hepatitis due to closure of the *ductus choledochus*, in which they have found similar changes of the inter- and intralobular gall-ducts; this group they separate, as *cirrhosis of biliary origin*, or *biliary cirrhosis*, from the ordinary cirrhosis, in which the proliferation begins in the vicinity of the interlobular veins.

As regards the remaining *pathologico-anatomical changes* in hypertrophic cirrhosis with icterus, the enlargement of the liver is the most noticeable; the weight amounts to between 2,000 and 3,000 grammes: the form of the organ is not perceptibly altered, the free margin is sharp, the outer surface often smooth, at other times studded with flattened prominences not larger than a small pea; the cut surfaces, whose color may be yellow or green in different shades, presents now and then somewhat prominent parenchyma-islets, varying in size from a hemp-seed to a poppy-seed, and between these islets are found cross-pieces of fibrous tissue broader than the former by four- and fivefold. The spleen, too, is invariably and, as a rule, considerably enlarged by chronic hypertrophy; it weighed frequently 500 grammes, once (Pitres quoted by Hanot, l. c., p. 35) 1,300, and once (P. Olivier) even 2,300 grammes.

The first *symptoms* of the disease consist occasionally, in the main, of derangements of the digestive function; more frequently, however, the pathological process announces its presence in a more direct way by pain in the hepatic region, which from time to time recurs and is accompanied invariably by an increase of the icterus and the hepatic swelling, as also in most cases by fever. In the mammary line the liver projects at least by the width of several fingers beyond the lower margin of the ribs; frequently it extends down as far as the navel or even

lower, and across as far as the spleen, in consequence of which the upper abdominal region may bulge outward, filling up both hypochondria. Any reduction in its volume appears, even where the affection is of quite long duration, extremely rare, occurring even then only to such an extent that it is still quite far from being diminished below the natural size. It frequently happens that, owing to the encroachment of the liver, the size of the splenic tumor cannot be accurately determined. The nutrition and general condition may continue for a long time very fair; at other times progressive emaciation and cachexia commence at even an early stage. Hemorrhages from the nose, too, occur occasionally even at an early date. Hemorrhages from the digestive organs are very rare. Symptoms of chronic catarrh of the mucous membrane of the digestive organs, on the other hand, when not existing from the beginning, appear uniformly at a later period. Ascites is at times absent even in patients already very far reduced; more frequently it appears as a concomitant of general dropsy induced by cachexia, not setting in until the œdema has mounted to the abdomen. Yet it often supervenes when no anasarca is present, but then usually not until the last weeks or months of life. Death is frequently ushered in by severe cerebral symptoms (delirium, coma, occasionally with ultimate increase of temperature).

The *duration* of the disease seldom amounts to less than a year—generally two years and over; in individual cases (P. Olivier, Pitres) it is stated to be five and seven years.

The morbid process here sketched is in many respects very similar to that which Hayem, generalizing from two cases observed by himself, has described as *simple hypertrophic cirrhosis.*

In these cases, also, the liver was very much enlarged, weighing in one instance 3,180, and in the other nearly 4,000 grammes; it presented a smooth surface and fibroma-like consistence. The lobules, which to the naked eye looked like differently colored spots and dots upon the grayish-white ground of the cut section, appeared on microscopic examination to be separate groups of cells, distributed partly in insular form in the interstitial tissue, dissolved and so changed in structure that the central vein was in the first case nowhere recognizable, in the second but partially so. In many lobules the capillary vessels were, either throughout or at certain

points, largely dilated. The connective tissue, very considerably increased, was composed of fibres and spindle-form cells, and exhibited, principally along the course of the vessels, a finely cellular infiltration. The hepatic cells were here and there atrophic—in the main, however, well-preserved, and infiltrated neither with fat nor with pigment. The interlobular gall-ducts appeared normal; in the second case some were filled with small pigment-concretions. In this case slight jaundice had existed for some time; in the other, toward the end of life, the skin began to assume a faint yellowish tinge (sub-ictérique). Ascites was absent in the second case, although the disease lasted two and three-fourths years: in the first, the duration of which was said to be nine years, it did not appear until after the œdema of the lower extremities; there was here formed, however, by means of the very wide vessels of numerous peritonitic adhesions, a direct communication between the veins of the intestine and the largely distended and tortuous veins of the anterior abdominal wall. In both cases the patients died in a state of marasmus: one of pneumonia, and the other of cholera.

In these cases, as well also as in those accompanied by the early development of icterus, the question naturally arises whether the circumstance, that the enlargement of the liver continues present until death, can be legitimately considered a criterion of an especial form of interstitial hepatitis. Inasmuch as the symptoms of obstruction in the system of the ramifications of the portal vein are usually but slightly developed, the idea of cirrhosis not fully completed is naturally suggested. In ordinary cirrhosis, moreover, the organ now and then presents a similar increase in volume and weight, when, in consequence of some complicating or intercurrent disease, death is induced before any very extensive shrivelling has taken place. In hypertrophic cirrhosis with icterus, one would be inclined to ascribe to the prolonged jaundice an accelerating influence upon the fatal termination. But apart from the fact, that no analogous agency is to be found in ordinary hypertrophic cirrhosis, the theory that we have here to do with an early stage of the process is, in both varieties, already disproved by the duration of the disease. This period in hypertrophic cirrhosis is by no means shorter, but generally even longer than in the ordinary form, and a duration of five years and over, which occurs—though rarely—in the former, has never been observed in the latter. Indeed, in one of the cases reported by Frerichs (loc. cit., p. 82, Obs. 19) the symptoms of chronic hepatitis had already begun six years previous to death;

but this was obviously not an instance of ordinary cirrhosis, for on post-mortem examination the liver was found still quite enlarged and heavy, the granulations very small, and the fibrous structure very abundant, the ascites being slight. But, furthermore, in hypertrophic cirrhosis the course of the affection tends to refute also the theory, that the sole reason why a consecutive diminution in the size of the liver has not taken place, is because the disease has not reached its last stage. The impairment of the general nutrition, which in ordinary cirrhosis keeps pace with the progressive shrivelling of the liver, is induced in the hypertrophic variety, although the enlargement of the organ continues or even increases, and without the intervention of any other disease not dependent upon the hepatic disorder and its *sequelæ*, to which the nutritive disturbances can be referred. To what these derangements are due, cannot be accurately determined. It is possible that the principal cause is the destruction of a large part of the secreting elements of the liver, necessarily attending the proliferation of the interstitial tissue; for while in ordinary cirrhosis the pressure of the shrivelling new-growth exerts its influence first of all on the finest ramifications of the portal vein, in the hypertrophic form the hepatic cells appear to suffer more directly under the proliferation of the connective tissue, which penetrates here much farther into the interior of the acini.

Respecting *etiology*, in this variety, also, mention should first of all be made of the habitual abuse of alcoholic spirits; according to P. Olivier, this forms, indeed, the sole well-established cause. Hayem's first case, however, justifies the assumption, that the first germ of the disorder may also be implanted by certain infectious diseases, such as typhus and cholera. Not unfrequently the cause is unknown. In no case has the presence of syphilis been demonstrated.

As regards the *diagnosis*, during its early stage the affection cannot be distinguished from ordinary cirrhosis. In the later period of its course, on the other hand, when the emaciation and cachexia have become more prominent, its recognition commonly offers no especial difficulties as soon as it is possible to definitely establish the long duration, extending frequently over a period

of years, of the hepatic and splenic enlargement, and, in the majority of cases, of the icterus. By carefully considering the normal form of the organ, and noting the absence in its vicinity of fluctuating or soft-elastic spots, we are enabled to guard against confounding the disorder with echinococcus, which has in some cases happened; moreover, echinococcus of the liver is followed by neither splenic enlargement nor cachexia. An erroneous assumption of the existence of leucæmia can be avoided by an examination of the blood. In pseudo-leucæmia the splenic enlargement is almost invariably relatively greater by far than that of the liver, and, with very rare exceptions, tumors of the lymphatic glands, too, are present. In contrast with carcinoma, the smooth condition and the uniformly equal resistance of the hepatic surface, as well as of the splenic tumor, should be taken into account. From amyloid degeneration, hypertrophic cirrhosis is distinguished by the sharp lower margin, and by the dissimilarity of the causes.

In the *treatment* of hypertrophic cirrhosis, no appreciable result whatever has been attained by any of the remedies hitherto tried (iodide of potassium, mercury, muriate of ammonia, arsenic, iron). The affection very rarely affords an opportunity for paracentesis of the abdomen.

Syphilitic Hepatitis.

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—*v. Baerensprung*, Die hereditäre Syph. Berl., 1864. S. 189 ff.—*H. Weber*, Transact. Path. Soc. Vol. XVII. 1866.—*W. Moxon*, Transact. Path. Soc. Vol. XXII. 1871, p. 274, and Vol. XXIII. 1872, p. 153.—*Oedmansson*, Nord. med. Arch. I. 4. (Virchow-Hirsch, Jahresb. f. 1869. 2. Abth., S. 561.—*Kahl*, Beitr. z. Anat. u. Symptomatol. d. syphil. Affect. der Leber. Leipzig. Dissert. 1869.—*Schueppel*, Arch. d. Heilk. Bd. XI., S. 74.—*Lancereaux*, Traité de la Syphilis. Paris, 1873, p. 259.—*Baeumler*, Dieses Handbuch. Bd. 3., S. 177 ff.—Compare, moreover, the Handbooks of Pathological Anatomy by *Foerster*, *Klebs*, und *Rindfleisch*.—For other literature of the subject, see also *Lancereaux*, loc. cit., pp. 258 and 259.

Historical Account.

The most ancient writers on syphilis maintained, on purely theoretical grounds, that the liver does not form the real seat and starting-point of the affection, and that it is not an organ which becomes at a very early period consecutively affected. As regards the pathologico-anatomical appearances which are cited by later authors (Bonet, Astruc, Baader, Van Swieten, Portal) as examples of syphilitic affection of the liver, their theory seems to rest upon a very questionable basis. In the description of "encysted nodular tumors of the liver," given by Budd in the first edition of his work on Diseases of the Liver, the gummata are not to be mistaken, but they were regarded by him as circumscribed dilatations of the inflamed gall-ducts, whose contents had undergone caseous transformation. Oppolzer and Bochdalek interpreted these same appearances as cancer of the liver which had healed. Dittrich pointed out the error of this view, and was the first to recognize with certainty the syphilitic nature of the change. With his work begins the more exact investigation of syphilitic hepatitis, which he first of all studied in adults. The observations of Gubler, published shortly afterward, were directed toward the analogous affection in children. Since then, numerous researches have contributed to our knowledge of the disease in its various forms.

Etiology.

In proportion to the widespread prevalence of syphilis, the affection occurs, no doubt, rarely; but of the syphilitic disorders

of the abdominal viscera it is one of the most frequent. Moreover, in hereditary syphilis the liver forms one of the organs most constantly attacked, and here, likewise, generally exhibits according to the experience of Gubler, v. Baerensprung, Wegner[1] and others, inflammatory changes; although Wilks[2] found in many autopsies nothing but fatty degeneration and thickening of the capsules.

The hepatitis induced by acquired syphilis is observed at a later period of the chronic infectious disease. As a rule, there are found associated with it alterations in other organs, which originate in processes of the tertiary stage, either completed or still going on, or which are dependent upon the syphilitic cachexia. Moreover, the appearances found in the liver are generally, in part at least, such as would be considered characteristic of the tertiary stage. In many cases, however, syphilis, even in an earlier period of its course, gives rise to interstitial hepatitis (Dittrich, Gubler, Leudet, Biermer). This probably occurs with greater frequency than is observed, since the process, especially when limited to smaller points of the liver, may continue quite unaccompanied by symptoms.[3]

Pathology.

It would be impossible to draw a distinct sketch of the disease; by what symptoms, if any, it is attended, depends principally upon the seat and extent of the *anatomical changes*, and in this respect the separate cases afford quite a manifold variety.

Syphilitic hepatitis, like cirrhosis, has its seat at the outset in the interlobular connective tissue; like the latter it tends to produce gradual wasting of the glandular parenchyma to a variable extent; and here, also, takes place a transformation of the

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[1] Virchow's Archiv. Bd. 50, S. 316 ff.

[2] Transactions of the Pathological Society. Vol. 17, p. 167.

[3] In the cadaver of a woman, aged twenty-six years, who six months previously had been treated for an ulcer of the external labium, and had died of miliary tuberculosis, *Key* (Hygiea, 35, p. 370; Schmidt's Jahrb., Bd. 161, S. 142) found as the only indications of syphilis two gummata of the liver of the size, respectively, of a walnut and a pea.

granular structure, rich in cells, into callous cicatricial tissue, in consequence of which even the changes in form resulting from both these processes afford manifold points of resemblance. They present, however, certain points of difference, which generally render a diagnosis easy, and characterize syphilitic hepatitis as a specific form of inflammation. The tissue developed in the liver by the action of the syphilitic poison tends in a high degree to fatty and caseous degeneration, and the products of this retrograde metamorphosis may be completely resorbed, in consequence of which the new-growth disappears, and in certain cases a cicatrix of moderate size alone points to hepatic syphilis.

The manifold variety, which, in an anatomical and symptomatological respect, is in general peculiar to syphilis, is displayed also in the diverse forms in which it appears in the liver; and herein lies the reason why many distinct varieties of syphilitic hepatitis have been recognized. In fact, they all represent but one process, whose different stages and whose appearance sometimes in circumscribed spots, and at other times diffused, must be duly considered when it is desired to make any particular case correspond to the general typical picture.

We recognize diffuse syphilitic hepatitis terminating in induration, and circumscribed, gummous hepatitis, or syphiloma of the liver, which in the latter stage, or after it has been comparatively healed, represents the so-called lobulated liver.

Diffuse hepatic syphilis is observed most frequently as a concomitant of congenital lues in still-born children, in such as die a few days or weeks after birth, and in the dead and putrid (*todtfaul*) fœtus; it is seldom found in adults. The liver is generally enlarged in all diameters and increased in weight,[1] of a reddish-gray, or dirty, yellowish-gray color, which is compared by Gubler to that of flint. Its outer surface is smooth, and not adherent to the surrounding structures. Its tissue is exsanguine, firm, faintly glistening, indistinctly acinous, or quite homogeneous—the latter even when no amyloid degeneration can be

[1] *Birch-Hirschfeld* (Archiv d. Heilk., Bd. 16, S. 174) found the average weight of livers of children affected with syphilis (thirty-two cases) 129 grammes, the normal weight being 109 grammes; or in syphilis 6 per cent. of the weight of the body, the normal relative weight being 4.6 per cent.

detected; frequently, as is stated by Gubler, it can be cut into thin sections with perfectly smooth, even surfaces, resembling in this respect, also, tissue that has undergone amyloid degeneration. Under the microscope, the interlobular connective tissue is seen to be almost everywhere broader and studded more or less abundantly with finely granular, roundish and spindleform cells. Small groups of round cells are found also within the acini, arranged in regular order around the capillaries, completely taking the place of the hepatic cells, or crowding into them to a variable extent, so that they appear flattened, and frequently afford evidence of different stages of simple and fatty degeneration. The newly-formed cells in the intra-acinous structure lie in the plainly perceptible connective tissue (Wagner, loc. cit., S. 140), which is developed either directly from the walls of the capillaries, or from the interlobular connective tissue situated along their course. We can often distinguish a structure rich in cells growing into the interior of the acini from the periphery.

The close resemblance presented by diffuse syphilitic hepatitis to the early stage of ordinary interstitial hepatitis, seems to justify the assumption, that when the affection is of long standing the liver must exhibit an appearance completely identical with the typical form of ordinary cirrhosis. Accurate observations upon this point, however, are wanting, and as regards those cases of granular liver observed in childhood, which cannot be referred to immoderate indulgence in alcoholic spirits, it is always doubtful whether they are to be regarded as cases of hepatic syphilis. On the other hand, a uniform induration of the liver with slight superficial granulation has been described as the result of diffuse syphilitic hepatitis.

This was once observed by Wagner in a man fifty-four years of age. "The liver was uniformly enlarged in all diameters, weighing six pounds, the outer surface tolerably smooth, *only in isolated spots finely cicatrized*, and of a peculiar yellowish-red tinge; *creaking when incised;* cut sections less distinctly acinous;" and so on. "The microscopic examination shows the *inter-acinous connective tissue, doubled in breadth*, and studded with uniformly distributed small and medium-sized granules and roundish cells." Another Observation is reported by L. Wronka.[1] In a fœtus,

[1] *Wronka*, Beiträge z. Kenntniss d. angeborenen Leberkrankh. Dissert. Breslau, 1872. Fall II.

aborted at the end of five months, he found the liver very small, six and five-tenths centimetres in transverse diameter, etc., the serous covering thickened and cloudy at many points. The organ felt quite compact and hard, and upon the outer surface was *slightly granulated.* An observation of Virchow, reported in his Archives (Bd. 22, S. 428), belongs probably to this class.

Between this diffuse affection of the liver and the gummous form, all possible modifications have been noted. White adherent patches, or minute points[1] of a yellowish tinge, are spoken of in the description of cases, which in other respects correspond to the diffuse variety. At other times, distinct *miliary tubercles* are found in great quantity, between which the hepatic tissue exhibits an almost normal consistence, or still presents a distinctly acinous structure. Such observations—with reference to new-born children almost exclusively—were reported first of all by Gubler, then by Wagner and Klebs. Wagner (Case XXXIV.) and Wronka (Case I.) observed numerous miliary new-growths in addition to large nodules. The histological structure of these minute syphilomata does not differ from that of the larger variety.

Circumscribed syphilitic hepatitis has often been observed in childhood, as well as particularly at a maturer age, and constitutes, in connection with the lobulated liver, which represents its terminal stage, the most frequent form of hepatic syphilis. There are commonly found in the hepatic structure, that in other respects is either normal, consecutively hypertrophied, or the subject of fatty or amyloid degeneration, one, several, or rarely many (fifty and over) gummous nodules, varying in size from a pea to a hen's egg.

The relative size is, in fact, quite variable; but the statements of different authors upon this point are also to be interpreted differently, accordingly as the cicatricial peripheral zone of the mass is regarded as belonging to the syphilitic new-growth, or as a secondary development of capsule.

These nodules have been occasionally found in almost every part of the organ—deep-seated and superficial, covered by the diaphragm, or at the projecting margins of the lobes. There seems to exist, however, at certain points a predilection for

[1] *Klebs*, loc. cit. Bd. I., S. 440.

their development: the vicinity of the suspensory ligaments of the liver, especially the *ligamentum suspensorium hepatis* and the areolar tissue of Glisson's capsule at the *porta hepatis* and along the course of the large branches of the *venæ portæ*. Virchow draws attention to the fact, that the traction of the weighty organ upon its suspensory ligament may possibly favor the formation of the new-growth at this point. As regards the other points of predilection, the reader is referred to the Observation of Schueppel, who narrates, under the title of "Syphilitic peripylephlebitis in new-born children," three cases of localization of the syphilitic new-growth around the portal vein.

He found the branch of the portal vein at its entrance into the liver transformed into a firm, yellowish-gray colored cord, one centimetre in thickness, the calibre of the vessel being so narrowed as to barely admit the introduction of a hog's bristle.

Schott, too, observed in certain cases of hereditary syphilis firm nodules around large vascular branches, from which whitish cicatrices radiated in different directions. If the nodules are superficially seated, the hepatic peritoneum is often forced upward as in secondary hepatic cancer, and exhibits recent inflammatory changes, or the effects of such changes, viz., cicatricial thickenings and adhesions with neighboring organs. It is comparatively seldom that syphilitic tumors of quite recent development come under observation. Upon section they are of a white, reddish, or gray color, of a marrow-like appearance, and tolerably firm consistence. In a finely or coarsely fibrillated connective tissue they contain, in addition to numerous round and spindle-cells, many vessels, principally capillary, and an oft widely ramifying network of gall-ducts with distinct cylindrical epithelium. The hepatic cells in their vicinity are atrophied, and, owing to the albumen- and fat-granules, cloudy. Upon the margin of the new-growth the progressing proliferation, chiefly in the interlobular connective tissue, may be traced along different broad streaks in the form of a fine-cellular infiltration.

Upon the cut surface of older and especially larger syphilomatous nodules there may usually be distinguished with the naked eye two substances, differing as regards their arrangement, color-

ing, and consistence. A central portion, presenting the yellowish color of inspissated pus or of tissue that has been converted into a cheesy substance, is tenacious and dry; it forms, for the most part, a body having an irregularly jagged, or roundish outline; frequently it appears upon section as a ramifying figure, or may assume a reticular form, suggesting to some observers the ramification of widely dilated lymphatic vessels. It consists of fine, thickly interwoven fibres, cell-detritus, fat-globules, so-called free granules, and a limited number of atrophic round cells lying scattered about. Accumulations of larger fat-globules, as well as the pultaceous or friable consistence which is elsewhere exhibited in tissues undergoing caseous degeneration, are commonly wanting.

It is in exceptional cases only that complete softening seems to occur; it was observed by Zenker (Baeumler, loc. cit., p. 180), Wagner (loc. cit., p. 123, Case 24), Moxon (Transactions of the Pathological Society, Vol. 23, p. 153). Cretaceous deposit in the centre of the nodules was found in one instance by Wegner (Berl. klin. Wochenschr., 1869, p. 420), and also by Wronka (loc. cit., p. 11); each case occurred in a fœtus of nine months.

The central portion of the new-growth is surrounded by an areola of varied width, composed of reddish-gray or cicatricial-like, dull-glistening tissue, which presents upon the side of the adjacent hepatic tissue a margin usually well-defined but irregularly jagged. This callous substance exhibits under the microscope the appearance of either recent or old cicatricial tissue, and, like the latter, is in a variable degree rich in vessels often conspicuous from the remarkable thickness of their walls (obliteration?), and consists chiefly of round and spindle form connective-tissue cells; the latter form generally the outermost zone of the tumors, whereas the roundish elements preponderate in the direction of the yellow substance, and may be invariably detected therein. There exists no sharp boundary between the two substances, of which fact one can be readily convinced by a microscopical examination; the callous tissue may be said to merge imperceptibly into the atrophic, and it would, therefore, appear also incorrect to regard the callous peripheral portion as merely the product of a reactive inflammation—as a capsule formation.

The transformation of the highly vascular granulation-tissue, of which the new-growth at first wholly consists, into a cicatricial tissue poorly supplied with vessels, is closely attended by the destruction of the cellular elements and the caseous degeneration which starts from the centre. The substance that has undergone caseous degeneration is gradually resorbed; the tumor is reduced in size, and ultimately forms merely an additional cicatrix of variable and generally radiating form in the hepatic tissue. If the new-growth was seated near the outer surface, then this follows the cicatricial retraction of the connective tissue, and there are formed irregular puckerings, generally deep, and supplied with lateral prolongations; between these depressions the remaining glandular tissue, that frequently has undergone amyloid degeneration—though it is, no doubt, often hypertrophic—is converted into semi-globular prominences. Ultimately the organ appears to be cleft by fissures into abnormally shaped lobes—lobulated liver. It is obvious that, according to the quantity and position of the tumors undergoing atrophy, the resulting deformities of the organ must present a manifold variety, especially if we consider also the further changes that may be induced by perihepatitis, abnormal adhesion with neighboring organs, and the diverse affections of the parenchyma which now and then appear, in part consecutive upon syphilis, and in part independent of that malady (simple atrophy, fatty and amyloid degeneration, acute yellow atrophy, hepatic hypertrophy). In cases where the development of the callous connective tissue in the periphery of the new-growth has attained an especially high degree, it has been doubted whether a complete resorption of the caseous mass can take place. The circumstance, however, that there may occur in one and the same liver characteristic cicatrices without any trace of cheesy deposit in their interior by the side of those which exhibit plainly the remains of syphilitic new-growths, appears to favor the above-described mode of retrograde development and the possibility of complete resorption. The question as to the resorption of the tumors in question is one of importance, not only as regards the anatomical comprehension of the process, but it presents also a practical interest, inasmuch as by the resorption and taking

up of the products of degeneration by the circulation, the infection of other organs may possibly be produced.

Symptomatology.

Syphilitic hepatitis makes its appearance and frequently runs its course without any symptom whatsoever pointing to disorder of the liver, even in cases where the autopsy reveals the presence of deep cicatrices and numerous gummata. Where, however, the disease gives rise during life to any phenomena, these may be due to changes in the physical properties in the organ, to the peri-hepatitis, and to the pressure of the fibrous tissue upon the blood and bile-vessels.

The *liver* rarely presents normal dimensions. In congenital cases it almost always appears enlarged in all directions, and forms a smooth and hard tumor, which may project downward with its sharp margin as far as the navel and even further, and is frequently traced against the abdomen by the bulging of the corresponding parts. These appearances may be present in acquired syphilis at an earlier stage of the hepatic affection. More frequently, however, the contour of the organ is irregular; upon its outer surface may be detected distinct protuberances or nodules, ranging in size from a walnut to a hen's egg, and now and then perceptibly pushing out the abdominal integument; these nodules feel smooth and generally hard, although the constricted portions of the liver may not have undergone amyloid degeneration; more rarely they have the doughy consistence of hepatic parenchyma abounding in adipose tissue (Frerichs,[1] Loewenfeld[2]); where they are more thickly situated, shallow or deep furrows[3] may be detected between them. The lower margin is

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[1] Loc. cit., Observation 20.

[2] Wiener med. Presse. 1873. Nr. 39.

[3] In the case narrated by *Riegel* (Deutsches Archiv f. klin. Med., Bd. XI., S. 113), the portion of the liver which was constricted and connected with the remainder of the organ by a long pedicle, appeared during life like two moderately hard and very movable tumors, not taking part in the respiratory displacements of the organ, and forming in the right side of the abdomen circumscribed regions of dulness, which were separated from one another as well as from the natural hepatic dulness by clear tympanitic, resonant zones, corresponding to the superimposed coils of the intestines.

usually blunt, and at times divided into numerous knotty, rounded segments. These appearances are most distinctly marked when the liver lies to a large extent in contact with the abdominal wall: the organ may dip down into the ischiatic region and far into the left hypochondrium (Quélet, Biermer); but even when it is, on the whole, reduced in size, there is also frequently found, in consequence of the irregular distribution of the shrivelling tissue, a prominent portion beneath or near the right margin of the ribs, upon which the above-described changes may be made out. According to Lancereaux, we can occasionally feel the adhesions that have formed, or we can determine their existence from the circumstance that the organ is not displaced beneath the abdominal integument upon respiration. The lesions observed in the liver usually continue essentially of a similar character even when kept under prolonged observation; it is but seldom that an opportunity is offered of demonstrating a gradual reduction in volume of the organ that at the beginning was enlarged, and the appearance thereon of protuberances.

Where the liver is increased in bulk there is experienced frequently a sensation of discomfort, weight or pressure in the right hypochondrium, which, no doubt, has its principal origin in the enlarged volume of the organ. At other times pain is present, either temporarily or continuing uninterruptedly for a period of weeks and months, sometimes extending over the entire hepatic region, at other times limited to separate spots; this pain may be quite violent, and is invariably aggravated by external pressure; less frequently it is first of all brought on by such pressure. In nursing children, we are often apprized of its existence by their sighs and the flexed posture of their legs. The pain is attributable to the peri-hepatitis. The existence of the latter lesion is also revealed occasionally, according to Gerhardt,[1] by a respiratory friction sound in the superior abdominal region, audible, and still more easily felt. Pain in the right shoulder and right arm is complained of by few patients only, notwithstanding the adhesions between liver and diaphragm, which are almost invariably present and generally quite firm.

[1] Lehrbuch d. Kinderkrankh. 2. Aufl. 1871. S. 464.

Ascites is developed frequently, but not solely, when the liver is unnaturally small (Schuetzenberger, Hjelt,[1] Niemeyer,[2] and others). It is frequently found, moreover, in hereditary cases, but chiefly, no doubt, in still-born infants, or those who have died shortly after birth (in five out of nine post-mortem examinations reported by Wegner[3]); by far less frequently among those who remain alive longer (in a child of seven weeks in Wagner's forty-eighth case; in a child of nine weeks in von Baerensprung's twenty-second case). It is due, as in cirrhosis, to the closure of numerous ramifications of the portal vein by the pressure of the new-growths in Glisson's capsule, and even here may be so considerable as to give rise to the enlargement of the superficial abdominal veins, to render quite difficult the examination of the liver, and by forcing upward the diaphragm to necessitate puncture; in a case not published, twenty-seven pounds of slightly hemorrhagic fluid were thereby released. *Hemorrhages from the mucous membrane of the stomach and intestine*, also arising from compression and consecutive thrombosis of the larger branches of the portal vein, sometimes occur (Leudet, Frerichs, Loewenfeld). The *diarrhœa* occasionally present is frequently attributable to amyloid degeneration of the intestinal mucous membrane.

Icterus is rare. Branches of the *ductus hepaticus* may, in consequence of the shrivelling connective tissue on the concave surface of the liver, undergo a cicatricial constriction; in such cases icterus may appear even at an early stage, become quite severe, and persist with slight fluctuations for many months. The secreting parenchyma in the fibrous mass is, however, generally destroyed. Frerichs maintains, as the result of his own observations, that in amyloid degeneration and in the formation of gummata in the liver icterus may also be induced by the perihepatitis and swollen portal glands.

The hypothesis of Gerhardt, that in syphilitic new-born children the oft-described formation of numerous ecchymoses upon the skin is also connected with

[1] Finska läkaresällskap handlingar. Bd. 11, S. 153. Schm. Jahrb. Bd. 161, S. 141.

[2] Lehrbuch d. Pathol. u. Therap. 9. Aufl. von E. Seitz. Bd. 1, S. 742.

[3] Virch. Arch. Bd. 50, S. 316 ff.

the jaundice, is contradicted by the circumstance that *ecchymoses* of the external skin, as well as of the serous membranes, the muscles, and various internal organs, occur also in like cases where icterus does not accompany hepatitis, or where the liver is usually not perceptibly affected. (Compare Wegner, loc. cit., Cases 1, 6, 12; von Baerensprung, loc. cit., Observations 11, 12, 50.)

Whether the icterus, which appears occasionally at an early period of the secondary stage of syphilis, though not generally persisting for a long time (Gubler, Leudet), is really related, at least in certain cases, to the hepatitis, cannot be determined from observations thus far communicated.

A case narrated by Biermer appears to support this idea. The patient, twenty-eight years old, infected nine months previously, exhibited severe general icterus, together with syphilitic roseola, and not an inconsiderable enlargement of the liver, whose outer surface, as well as the spleen, felt hard and covered with small protuberances; under the use of iodide of potassium the icterus diminished pretty rapidly, and then disappeared, leaving but a trace behind, whereas the objective changes of the liver underwent no perceptible modification.

The majority of patients present a dirty, pale, earth-colored *skin;* yet, according to Lancereaux, bronzed skin is a quite frequent symptom in hepatic syphilis, and in Schuetzenberger's case, as well as in the two cases reported by Pleischl and Klob,[1] occurring in Oppolzer's clinique, relating to girls aged twenty-eight and twenty-nine, a pale-brownish coloration of the entire integument is described.

Hepatitis syphilitica is, as a rule, accompanied by a distinct and at times quite remarkable *splenic enlargement*, originating either in hyperplasia, gummatous growths, or amyloid degeneration of the organ; where one of the first two lesions is present, the region of the spleen appears at times sensitive to pressure.

Albuminuria, also, and the secretion of hyaline or epithelial casts with the urine, occur frequently as symptoms of parenchymatous and amyloid degeneration of the kidneys.

As regards the *diagnosis*, characteristic syphilitic processes in other organs, or remains of such processes, are naturally of the greatest importance: apart from the exceptional cases, where the hepatic disease comes under observation even in the

[1] Wiener med. Wochenschrift. 1860. Nr. 8, 9.

stage of the roseola and of the condylomata, there are found most frequently cicatrices upon the genitals; cicatrices and ulcers of the soft palate, pharynx, trachea; swelling of the cubital, inguinal and cervical glands; specific affections of the bones of the skull, nose, hard palate, tibia, clavicle, ribs; sarcocele, ulcerative syphilides, etc. In exceptional cases, however, all such indications as to the nature of the hepatic affection are wanting, under which circumstances its recognition may present great difficulty, inasmuch as we can scarcely avoid mistaking it for cancer of the liver,[1] or non-syphilitic cirrhosis. As affording a means of distinguishing between the protuberances of the syphilitic lobulation and projecting cancerous nodules, importance is attached by Frerichs to the consistence; in the latter affection, this, he affirms, is invariably changed; in the former, on the other hand, it resembles that of the normal hepatic tissue; yet in both affections, in the majority of cases, the tumors seem firm to the touch. Lancereaux, indeed, ascribes to the nodular elevations on the outer surface of the syphilitic liver a greater firmness than to those due to carcinoma of the liver. According to the last-mentioned observer, the former are distinguished from the latter by their more distinctly circumscribed outlines; it would be scarcely possible, however, in any given case, to turn to account any such relative difference. Moreover, apart from the circumstance that at times carcinoma, likewise, affects chiefly one lobe, viz., the left, in consequence of which the increase in volume may be limited to that lobe, it is only in very rare cases that it will be possible to determine with certainty during life the disproportion between the size of the separate lobes, which Lancereaux likewise maintains to be characteristic of hepatic syphilis as distinguished from carcinoma. Bamberger directs attention to the fact that the protuberances remain for a long while stationary, and that their outline is less uniformly round; but the separate divisions of the lobulated liver not unfrequently form almost perfect segments of a sphere, and as by the increasing shrivelling of the surrounding tissue they project more conspicuously, they seem to increase in size; or, at other times, by hypertrophy of

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[1] Vide *Virchow*, Die krankh. Geschwülste. Bd. 2, S. 428.

the hepatic cells, they do actually become enlarged. A far more reliable clue is afforded by the comportment of the spleen, the enlargement of which is quite as uniformly present in syphilitic hepatitis, as it is wanting in carcinoma of the liver. In like manner, as regards the differential diagnosis, the frequent occurrence of albuminuria in hepatitis syphilitica deserves consideration. Occasionally, also, the age of the patient may be, to a certain extent, of importance as affecting the decision, in so far as one-half of the cases of hepatic syphilis occur in individuals below the age of forty, whereas, as is well known, cancer of the liver is relatively rare with such persons.

When the affection is attended by the complex symptoms of cirrhosis, in the absence of other indications of constitutional trouble, we shall frequently be put upon the right track by the circumstance that the diminution in size does not proceed at so uniform a pace as in ordinary cirrhosis, this being, for instance, more advanced in the right lobe than in the left; or, at other times, large, isolated protuberances may become prominent upon the outer surface, which is elsewhere covered with nodules.

The *course* of syphilitic hepatitis is insidious; it is always present for a longer or shorter period before giving rise to any symptoms. The theory enunciated by Rindfleisch—that the disease, having originated during fœtal life, may remain latent for a period of years without manifesting its presence until late in childhood, or about the time of puberty, as a result of which a portion of the cases of cirrhosis occurring at this period of life, the etiology of which would otherwise be completely obscure, should be referred to this origin—is, to say the least, a doubtful one. Quite as little proof has been afforded, that—as is maintained by Dittrich to be probable, in three cases reported by him relating to a lad aged eleven years, and to two girls aged fifteen and eighteen years—in congenital syphilis the hepatic affection may not break out until this period of life. The *duration* of syphilitic hepatitis may be protracted for several years after the appearance of the first symptoms. If the majority of cases result in a fatal termination within a much shorter period, this is due chiefly to the simultaneous action of other lesions co-existing with the hepatic affection. The influence exerted by this

affection itself upon the development and duration of any particular case of syphilis depends principally upon two circumstances: 1. Upon the permeability of the ramifications of the portal vein; the more this is impaired, by so much the more does the hepatitis become directly dangerous to life as a result of ascites, or of hemorrhage of the stomach and intestine. 2. Upon the amount of the glandular parenchyma still capable of performing its functions; but in this respect the amyloid and fatty degeneration, which is frequently coexistent, is of decidedly more importance than the hepatitis. Indeed, to fatty degeneration is also to be credited the death that takes place in certain cases under symptoms of icterus gravis. New-born infants die, as a rule, at the expiration of a few hours or days; it seldom happens that they survive until the second month, and only exceptionally until the third, in which case they frequently succumb to exhausting diarrhœa or acute general peritonitis.

The *prognosis* of the disease is, however, especially when acquired syphilis constitutes its origin, not absolutely unfavorable. The possibility of recovery, so far as this can be brought about by arrest of the proliferation, and by disintegration and resorption of its products, must, in view of our experience with reference to analogous changes in other organs, be *à priori* admitted. And, as a matter of fact, in the bodies of syphilitic patients who have died of another disease, there is here and there found a liver with firm cicatrices and irregular furrows in which no trace of any recent process can be detected. These cases, however, are for the most part, indeed, composed of those in which the hepatic affection had run a latent course. But occasionally, even in cases where the malady has given evidence of its presence by unequivocal symptoms, a portion of these symptoms—such, for instance, as the sensitiveness of the liver, enlargement of the organ, icterus—have been seen under antisyphilitic treatment to materially diminish or entirely disappear. These results have for the most part been attained by the internal administration of preparations of iodine (iodide of potassium, or, in case of greater anæmia, iodide of iron) (Frerichs, Kaesbacher,[1] Biermer, Oppol-

[1] Wiener medic. Wochenblatt. 1861. Nr. 36.

zer); and yet observations are not wanting according to which the employment of quicksilver, especially the gray ointment, has afforded a similar result (Schuetzenberger, Leudet, Duchek[1]). It is, indeed, true that there have not as yet been recorded any examples of a permanent removal of all the morbid symptoms, but a timely anti-syphilitic treatment may unquestionably arrest the process in its further development, and postpone the danger impending from this source. Among other cases that reported by Schuetzenberger will serve to illustrate this fact.

The woman, thirty-nine years of age, had ulcers of the pharynx, squamous syphilides, dolores osteocopi, periostitis tibiarum, dull pains in the right hypochondrium, and an appreciable enlargement of the liver; after a three weeks' treatment by inunction the remaining symptoms disappeared, and the volume of the liver was somewhat diminished. During the succeeding two years the condition of the patient was perfectly satisfactory; but at the expiration of that period the pain in the hypochondrium recurred, persistent icterus supervened, and eighteen months later enormous swelling of the liver, ascites, and a splenic tumor were found. Mercury and iodide of potassium now proved ineffectual; at the expiration of four months the patient died.

A cachectic appearance should not deter the physician from an energetic causal treatment. Where, however, marasmus of an advanced degree, or severe ascites depending upon the hepatic disease exists, then a dietetic-strengthening and symptomatic treatment is alone appropriate.

Acute Atrophy of the Liver.

Hepatitis Diffusa Parenchymatosa (Frerichs). Hepatitis Cytophthora (Lebert).

Morgagni, De sed. et causis morb. Epist. 37. 2, 6.—*Cheyne*, Dublin Hosp. Rep. Vol. 1, p. 282.—*Marsh*, Ibid. Vol. 3, p. 205.—*Martinet*, Biblioth. médic., Vol. 66; *Horaczek*, l. i., c., S. 120.—*Abercrombie*, Patholog. und prakt. Untersuch. From the English. 2. Th. Bremen, 1830. S. 445.—*Aldis*, Lond. Med. Gaz. 1834. Vol. 13, p. 833.—*Alison*, Edin. Med. and Surg. Journal. 1835.—*Bright*, Guy's Hosp. Rep. Vol. 1, p. 604.—*R. Froriep*, Pathol.-anat. Abbild. Lief. 1. Weimar, 1836. Taf. VI.—*Heyfelder*, Heidelb. medic. Ann. Bd. 4, H. 2.—*Scherer*, Würtemb. Correspondenzbl. 1841. S. 609.—*Rokitansky*, Handb. d. pathol. Anat. Bd. 3. Wien, 1842. S. 313. Lehrb. d. path. Anat. Bd. 3. Wien, 1861.

[1] *Chvostek*, Wiener medic. Wochenblatt. 1863.

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Historical Account.

The association of jaundice with severe brain symptoms, sometimes terminating fatally, was recognized even in the time of Hippocrates. By the surgical writers of the seventeenth century (Vercelloni, Rubeus, Baillou, and Bonnet) cases of this character are described; and, moreover, statements are even made, here and there, concerning the color of the liver, which, to say the least, justify the assumption that they relate to the disease now under consideration. But Morgagni was the first to communicate an observation of Valsalva which, according to the symptoms as well as to the appearances found in the cadaver, belongs, in all probability, to this category. More attention has been paid to the disease since the second decade of our century, chiefly, indeed, on the part of English surgeons, by whom also the first mention is made of the striking diminution in the volume of the liver. It was Rokitansky, however, who, above all others, by a description of the yellow atrophy of the liver as a specific, anatomically well-characterized form of disease, gave (1842) the stimulus to further investigations. In the following year appeared the monograph of Horaczek, which contains,

however, much matter decidedly foreign to the collection of cases forming the groundwork of the article. An important advance in our knowledge of the nature of the disease is marked by the discovery of the destruction of the hepatic cells, first demonstrated by aid of the microscope by Busk (*vide* Budd, l. c., p. 226), in the year 1845. During the last half-century, physicians elsewhere have also begun to search more thoroughly into the histological relations of the disease. These have formed the subject of accurate observations, first by Buhl, who was foremost in directing attention to the participation of the heart and kidneys; then by Robin, Zenker, Klob, and, later, Liebermeister, Waldeyer, Klebs, Riess, Bollinger, and others. Our knowledge of the clinical phenomena has been afforded principally by German observers, among whom Oppolzer, Bamberger, Frerichs, Wunderlich, Traube, Riess, and Schultzen, are especially deserving of mention in this connection; but in addition to this, the remaining cases reported from Germany and other lands, have also furnished many a valuable contribution to the symptomatology of the disease. Independent of recent treatises on diseases of the liver in general, comprehensive descriptions are contained in the works of Lebert, Demme, and Liebermeister. The theories that have been put forward respecting the nature of acute atrophy of the liver and its relation to other similar affections, will be discussed later in the pathological division of this treatise.

Etiology.

Acute atrophy of the liver is one of the rarest diseases; even in large hospitals it often fails to come under observation for a period of years.

It may make its appearance either primarily, and, to all appearance, independently, or it may be developed as a sequel to other diseases in which the liver is idiopathically or symptomatically affected.

The number of primary cases reported in detail which I have discovered in the literature at my command, and have made the chief basis of my description, amount to 143; they include, it is true, only those in which the diagnosis appeared

to me to be completely verified by the results of an autopsy. But, in addition to these, in the annual reports of hospitals and lying-in establishments, as well as in certain treatises on the disease, and especially those relating to its pathological anatomy, many other cases are barely alluded to; but, even if these, too, are included, the sum total of the observations hitherto reported would not much exceed two hundred.

The influence of *age* and *sex* upon the occurrence of the disease may be ascertained from the following table, for which primary cases have been exclusively selected.

Individuals.	Under 1 year.	1–4 years.	5–9 years.	10–14 years.	15–19 years.	20–29 years.	30–39 years.	40–49 years.	50–59 years.	60–69 years.	Age not given.	Total.
Male	1	5		2	8	21	8	7	1	1	1	55
Female	1	1		2	11	49	15	1	3		5	88
Pregnant women					1	16	10				3	30
Lying-in women						2					1	3
Total	2	6		4	19	70	23	8	4	1	6	143

It will be remarked that almost exactly one-half of the cases occur during the third decade of life, and three-fourths—at least 112, but besides these probably four others (the three pregnant women and one puerperal woman) whose ages are not indicated—occur at the period of from sixteen to forty. Before and after this period, embracing the prime of life, the frequency diminishes quite rapidly. It seems remarkable that the disease has never been observed in children between the ages of five and nine years, whereas the period of the first five years is represented by nine cases. One of these cases reported by Pollitzer, in which the appearances of the disease were very distinctly portrayed both during life and in the cadaver, occurred in a female infant who was taken ill on the fourth day after birth.

The remaining eight cases are found in Horaczek (Observation 38), in the report of the Joseph-Kinderhospital, in Gaupp, Heschl, Fagge, Loeschner, Mettenheimer, and Rehn. Moreover, an instance is reported by Hecker (Monatsschr. f. Geburtsk., Bd. 29, S. 334), where, in a new-born child, dying ninety hours after birth, the autopsy revealed the existence of fatty degeneration and reduction in the volume of the liver, as well as molecular disintegration of the muscular tissue of the heart and of the epithelium of the kidneys.

As regards sex, the females predominate very decidedly, there being fully one-half as many more cases among them than among the males; and, if we consider solely the period of maximum frequency, double the number (at least 75 to 37).

Among the seventy to eighty women passing through the procreative period, there are thirty pregnant and three in childbed. *Gravidity* manifestly induces, therefore, a predisposition to the disease in question. Of the pregnant women, three were at the time of their seizure in the fourth month, five in the fifth month, six in the sixth month, eight in the seventh month, one in the eighth and ninth month respectively, and six in the tenth month. The disease makes its appearance, therefore, in every stage of pregnancy excepting the first three months,[1] but most frequently about the middle of that period. Of the lying-in women, one was attacked in the first, one in the third, and one in the fifth week after confinement at full term.

Notwithstanding the predilection exhibited by the disease for pregnant women, still, even in cases of this class it is of very rare occurrence. Spaeth observed it in but two out of 33,000 cases of childbirth, and C. Braun in but one out of 28,000.

No other predisposing factors are recognized, or at least their existence has not been positively determined.

The theory that the disease, as was affirmed by Oppolzer,[2] occurs more frequently in the spring-time than during the other seasons, is not confirmed by the collection of eighty-one cases in which the date of the attack is given. Of these, nineteen occur in winter, twenty in the spring, eighteen in summer, and twenty-four in autumn.

Even the *physical constitution* and the previous condition of health appear to exercise no influence. For the most part, it is well-nourished persons who are attacked, and far more frequently robust than delicate individuals. Still, persons are occasionally seized who have been enfeebled by grief, destitution, or a dissolute course of life. In seven cases the previous history showed that the patient had already, upon one or more previous occasions, been *jaundiced;* but the number of these cases is manifestly too slight to constitute a basis for the theory, that in certain individuals there exists an especial predisposition to diseases of the liver or

[1] *Spaeth* (Wiener medic. Wochenschr., 1854, Nr. 49) relates a case occurring in the third month.

[2] According to the statement of *Pleischl* and *Folwarczny*. Zeitschr. d. Ges. d. Aerzte zu Wien. Bd. 14, S. 628.

of the gall-ducts, by which the development of acute atrophy is favored. In thirteen cases it was *topers* who were attacked by the disorder; and eight occurred in individuals who had either previously had, or were still subject to, *syphilitic* affections. Whether, in view of the above, a predisposing influence can be ascribed to the habitual abuse of alcohol and to syphilis, is generally—so far as may be judged from the frequency of its occurrence—at least questionable.

It is usually impossible to ascertain any especial *cause* of acute atrophy of the liver. In only about one-tenth part of the cases did the disease begin immediately after a severe, depressing mental emotion, such as vexation, fright, or anger; once (Breithaupt) after a very marked disrelish for a meal. Six cases, all occurring in topers, had been immediately preceded by unusual excess in the indulgence of spirituous liquors, and in two of these instances it seemed not unreasonable to assume that the disease might be the direct result of an acute poisoning with concentrated alcohol. (In one case, reported by Oppolzer, the patient had drunk a pint of rum; and in the other, reported by Leudet, a large glass of concentrated alcohol.) Still, as is recorded by Liebermeister, the experiments with acute alcohol-poisoning upon rabbits, instituted by Kirchner at the suggestion of the former, have afforded, as respects the liver, but negative results.

As a *secondary* process, acute atrophy of the liver occurs occasionally in cirrhosis of the liver, associated with long-continued biliary obstruction due to occlusion of the large excretory ducts, in fatty degeneration of the liver, and also, according to Traube's theory,[1] in other chronic affections of the organ; for example, in the changes induced by mechanical obstruction of the blood consequent upon heart diseases.

Cases in which acute atrophy is superadded to *cirrhosis* are reported by Loeschner, l. c., Observ. 2; Frerichs, Klinik, Bd. 2, S. 11, Beob. 1; Wunderlich, Arch. d. Heilk., Bd. 1, S. 23, Beob. 7; Liebermeister, Beiträge, S. 62, Beob. 14; Gee, St. Barthol. Hosp. Rep., Vol. 5, p. 103; Bollinger, l. c., S. 156; Picot, Jour. de l'Anat. et de Physiol., Vol. 8, p. 246; Maggiorani (Gaz. clin. di Palermo, 1874, Maggio, p. 193); Virchow-Hirsch's Jahresber. f. 1874, Bd. 2, S. 259. Examples of acute degeneration of the parenchyma of the liver in case of long-persistent biliary obstruction are found in Pleischl u. Folwarczny, Zeitschr. d. Wien. Aerzte, N. F., Bd.

[1] Berl. klin. Wochenschr. 1872. Nr. 19. S. 223.

1, Beob. 1; Demme, l. c., S. 234, Beob. 2; Murchison, Transact. of the Patholog. Soc., Vol. 22, p. 159. Instances of acute atrophy occurring in chronic fatty degeneration are reported by Frerichs, Klinik, Bd. 2, S. 14, Beob. 2; Wunderlich, l. c., S. 218, Beob. 15; Liebermeister, Beiträge, S. 185, Beob. 39; Bollinger, l. c., S. 154, and others. It is probable that to this category belong also many of the cases described as acute steatosis of the liver, *e. g.*, the first Observation in Stehberger.

Furthermore, the granular degeneration of the hepatic cells, which forms an alteration uniformly present in the majority of the *acute infectious diseases*, may exceptionally attain so high a degree in some of these affections—such as puerperal fever, recurrent fever, abdominal-typhus (typhoid fever)—that an acute wasting of the liver is thereby produced.

Buhl observed (Hecker u. Buhl, Klinik der Geburtsk., S. 244) in a form of *puerperal fever*, described by him as pyæmia associated with peritonitis, parenchymatous degeneration of the liver in every stage, even to a most typical picture of acute atrophy of the liver. Two cases of puerperal peritonitis are, likewise, reported by Hugenberger (l. c., Nos. 3 and 4), where the liver presented all the characters of acute atrophy. In the epidemic *recurrent fever* at St. Petersburg, in 1864, Kuettner (Herrmann and Kuettner, Die Febris Recurrens in St. Petersburg, Erlangen, 1865) found in several cases the liver of a consistence resembling perfectly that presented by the organ in acute atrophy. Similar lesions have been described by Frerichs (l. c., Bd. 1, S. 222, Beob. 18) in sporadic cases of *typhoid fever;* by Oppolzer (Wiener medic. Wochenschr, 1858, S. 448); Liebermeister (l. c., S. 207, Beob. 47); C. E. E. Hoffmann (Untersuch. üb. die pathol. anat. Veränd. d. Org. bei Abdominaltyphus, Leipzig, 1869, S. 214, Case 49); and Eppinger (Prager Vierteljahrschr. Bd. 118 u. 119, S. 51). Liebermeister (l. c., S. 332, Beob. 61) observed the development of the disease in a man, sixty-three years old, during the course of a catarrhal fever with ultimate croupous pneumonia.

In acute *phosphorus poisoning*, also, in certain cases running a less rapid course than usual, the liver ultimately undergoes precisely the same alterations as in well-developed acute atrophy.

Examples are found in Mannkopff, Wiener med. Wochenschr., 1863, Spitalzeit., No. 27; Bollinger, l. c., S. 149; Schultzen u. Riess, l. c., S. 8. Compare, also, Lebert et Wyss, Arch. gén. de Méd., 1868, Vol. 2, p. 267.

As in the last-mentioned categories of secondary development of the disease, the process which leads to the acute wasting of the liver is ascribed to the action of the infectious matter or poison, so, also, in the primary cases, so obscure as respects their etiology,

it has been conjectured that some analogous noxious influence forms the cause. However justifiable this idea may appear from a theoretical standpoint (*vide* under "Theory"), in no primary case has the existence of such a noxious influence been with certainty demonstrated.

According to the views of Gerhardt,[1] most cases of acute atrophy of the liver are dependent upon "acute *septic infection*, proceeding particularly from dead fœtuses within the uterus." Apart from the circumstance that the origin here particularly assigned to the supposed septicæmia is not at all met with in quite a large fraction of the cases, there are comparatively many, even among the women coming under observation who were pregnant or in childbed, from whom such a mode of origin is excluded. Of the thirty cases referred to in the above table occurring in pregnant women, in five a living child was born (Bamberger, Valenta, Beob. 2, Kowatsch, Beob. 1 and 2, Chamberlain); in two the fœtus did not die until the confinement (Hecker, Kiwisch); in one the heart's sounds were heard twenty-four hours after the appearance of icterus (Mettenheimer); in four cases it was distinctly stated that the fœtus was in a fresh condition (Frerichs, l. c., Bd. 1, Beob. 15, Davidson, Valenta, Beob. 1, Roper); and in the greater number of the remaining cases the existence of the opposite condition is improbable, for, considering the accuracy with which the cases referred to are reported, it may be fairly assumed that it would not have escaped mention if the fœtus had exhibited traces of decomposition; and, moreover, in the report of the autopsy, the uterus is frequently described as well-contracted and its mucous membrane as normal. At the same time it cannot, of course, be questioned that septicæmia, proceeding from the macerated fœtus, or from a putrid placenta, or from the remains of the fœtal membrane, may give rise to parenchymatous degeneration of the liver, with more or less extensive destruction of the secreting-cells. Bamberger,[2] Hecker,[3] Liebermeister (l. c., Beob. 43) and others have reported such cases.

The idea that the cause of idiopathic acute atrophy of the liver is attributable to the influence of a *miasma* derives support from certain observations, according to which the disease at times—varying from its usual sporadic occurrence—attacks simultaneously, or one after the other, several individuals dwelling together, such as members of the same household,[4] or persons upon the same ship.[5] Among these cases would be ranked, as

[1] Ueber Ict. gastro-duod. in Volkmann's Samml. klin. Vortr., Nr. 17, S. 3.

[2] Deutsche Klinik, 1850, S. 98, f. Beob. 2.

[3] *Chiari*, *Braun*, and *Spaeth*, Klinik der Geburtsh. Erl., 1855. S. 254. Beob. 3 and 4.

[4] *Griffin* bei *Budd*, l. c., S. 228. *Hanlon*, Ibid., S. 231. *Duckworth* u. *Legg*, l. c.

[5] *Budd*, l. c., S. 224—228.

respects the etiology, many instances occurring during epidemics of icterus, when associated with—as is quite probable as respects some of them at least—a rapid wasting of the hepatic parenchyma.

Epidemics of icterus in which certain patients—usually comprising exclusively or principally pregnant women—presented symptoms suggestive of the idea of acute atrophy of the liver, have been doubtless repeatedly observed;[1] but in one such epidemic only (*vide* note below, under 5) is there given any report as to the post-mortem appearances presented by the eleven cases that terminated fatally. Here the liver exhibited in all a uniformly yellow color and considerable anæmia; in two in addition to this, softening, and in one of these diminished volume and weight. The kidneys were decolored, enlarged, and friable; the spleen was in ten cases softened; but here, also, no microscopic examination of the organs was made.

Pathology.

General Features of the Disease.

In most cases the disease resembles, at the outset, an acute gastric catarrh; it is characterized by loss of appetite, a sensation of pressure at the epigastrium, vomiting, headache, languor, mental depression; the tongue is coated, the bowels, as a rule, inactive; moreover, moderate fever may be present, especially during the first days. To these symptoms are superadded, usually very soon—less frequently not until the lapse of several weeks—jaundice, which, in its manifestations, presents nothing different from catarrhal icterus.

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[1] In the list of these epidemics here appended, of the numbers adjoining in parenthesis, the first relates to the total number of cases occurring; the second to those which terminated fatally under symptoms of *icterus gravis*. 1. Epidemic at Lüdenscheid, 1794, described by *Kerksig*, Hufeland's Jour., Bd. 7 (70, † 3, 2 of whom were pregnant females). 2. At Greifswald, 1807 and 1808, described by *Mende*, Hufeland's Jour., Bd. 31 (?, † 2 : 1 toper, and 1 woman in the sixth week after confinement). 3. In the vicinity of Roubaix (Lille), in the beginning of the year 1850, described by *Carpentier*, Revue médic.-chir. Mai, 1854 (?, † 11 pregnant women). 4. At Martinique, 1858, described by *Gallot*, Gaz. des. Hôp., 1859; No. 62, and by *Saint-Vel*, ibid., 1862; No. 135 (spread over the entire island; possibly yellow fever, ?, † 20 pregnant females). 5. In the prison of Gaillon (Eure), 1859, from observations of *Carville*, described by *Bergeron*, Union médic., 1862 (47, † 11). 6. At Limoges, 1859–60, described by *Bardinet*, Union médic., 1863; No. 133, 134 (13 pregnant women attacked, of these † 3).

The derangements above mentioned, during the continuance of which the general condition of the patient is often so slightly affected as not to prevent attendance to the usual occupations, constitute the prodromal stage. The duration of this stage varies in the great majority of cases from several days to several weeks; it may, however, be protracted to a still longer period; and, on the other hand, may be limited to a few hours.

From the first stage the disease passes—quite suddenly, or attended by a more gradual development of nervous symptoms—into the second, the beginning of which is reckoned from the outbreak of severe brain-symptoms. The patients become somnolent, fall into a delirium, manifest great uneasiness, which, increasing in paroxysms, often amounts to insanity. Repeated vomiting usually takes place. Moreover, cramps of the voluntary muscles not unfrequently occur, which are oftener clonic than tonic. As a rule, sopor very soon supervenes, and ultimately coma. In quite exceptional cases only does the disease fail to advance to such severe cerebral symptoms, the patients exhibiting merely a constantly increasing weakness, apathy, and depression.

In many instances, even before the beginning of the second stage, but generally not until its subsequent course, a rapidly progressing reduction in the area of hepatic dulness may be detected, the meaning of which, as indicative of corresponding diminution in the size of the organ, is only in comparatively rare cases rendered uncertain by coexistent meteorismus. It may also happen, however, that no appreciable diminution in volume appears; indeed, in consequence of a combination with other pathological processes (fatty infiltration, interstitial hepatitis), the organ may be even enlarged. Sensitiveness of the hepatic region, or also of the entire abdomen, is frequently present, occasionally even in coma; but this is by no means a constant symptom. The splenic dulness is, as a rule, increased. In many cases vomiting of blood ensues, less often bloody stools, hemorrhages from the nose, hæmaturia, and discharges of blood from the mucous membrane of the mouth; not unfrequently petechiæ or ecchymoses in the skin are formed. In pregnant women, childbirth, which with rare exceptions

supervenes during the disease, commonly gives rise to metrorrhagia.

The urine contains, in the majority of cases, besides the abnormal constituents having their origin in the icterus, tyrosin, leucin, and the kindred products of deranged metamorphosis of tissue, and occasionally, also, albumen, pigment and granular epithelium from the urinary organs, and casts. The quantity of urates is much diminished, and may ultimately disappear completely.

At the outset of the second stage the pulse may present a normal rate, or—corresponding to the degree of the icterus—a diminished frequence; or, again, an increased, and then at times rapidly diminishing rate; later, however, it exhibits a uniformly increasing acceleration with diminishing volume. The temperature is normal, or somewhat below the normal point, and either remains thus until the last, or it may ultimately experience a more or less decided increase.

After the appearance of the severe symptoms but few days usually intervene before, in the deepest coma, or under symptoms of œdema of the lungs or of collapse, death ensues. It would appear, however, according to certain observations—not absolutely unquestionable, it must be admitted, as respects the diagnosis—that a termination in recovery may occasionally take place.

Anatomical Changes.

In well-marked cases the liver is considerably reduced in size, and relaxed to such an extent that it is found collapsed against the spinal column, with coils of the intestine superimposed. Most statements respecting the degree of wasting are based upon an estimate, according to which the volume may be reduced to two-thirds, one-half—indeed to almost one-quarter of the normal size. But a similar result is also afforded by the weights taken, first of all, by Bright, and more recently by numerous others: in thirty-three cases occurring in individuals in the prime of life the weight of the liver amounted to between 1,000

and 500 grammes; in a girl, thirteen years of age, 390 grammes.[1] The diminution in size chiefly affects the thickness. This reduction amounts, at times, in the left lobe, to not much over one centimetre (Frerichs, Foerster, Hugenberger, $\frac{1}{2}''$; Schultzen and Riess, scarcely $\frac{1}{2}''$); and even in the right lobe may be limited to a few centimetres (Ruehle, $1\frac{1}{4}''$; Frerichs, $1\frac{1}{6}''$). The organ is correspondingly flattened out, its edge being sharp, and, at times, almost as thin as a leaf.

In consequence of the reduction of volume and the extremely flabby state of the parenchyma, the capsule is rolled together in fine folds, presenting a cloudy, wrinkled appearance.

As regards the color and consistence, there exist manifold diversities, according to which the cases may be arranged in two groups. One of these groups comprises those instances in which the atrophic organ exhibits throughout a similar character, namely, a *yellow* color and great softening; whereas in the other class the *yellow* soft spots alternate with those *red* and relatively firm and tough.

In the cases of the former class the entire liver, especially upon the cut surface, appears intensely jaundiced; its color is gamboge, saffron, ochre, or rhubarb-yellow, according to the greater or less degree of anæmia of the tissue. At the same time, the outline of the lobules has either entirely disappeared, or seems, at least, as if partly obliterated. The acini, indistinctly separated from one another by a gray peripheral zone, are, as a rule, smaller than usual. Of the smaller blood-vessels little or nothing can be detected, owing to the small quantity of blood contained within them. Such a yellow liver is always extremely soft, yielding readily to pressure, easily ruptured, and at points almost pulpy. Upon microscopic examination there will be detected here and there, and most readily in the right lobe, hepatic cells still well preserved and colored yellow by diffused gall-pigment; still, the bulk of even these are without sharp contour, and present more or less granular cloudiness.

[1] The somewhat heavier weight (1,200 to 1,300 grammes) found in certain cases of very far advanced atrophy might be attributed to a proliferation (pre-existing or progressing simultaneously with the parenchymatous degeneration) of the interstitial tissue (*vide* farther on).

The alteration is commonly least marked in the centre of the acini, increasing toward the periphery; the gray peripheral zone consists almost entirely of minute granules and oil-globules. At numerous points, however, often especially in the entire left lobe, one can no longer detect the hepatic cells, but only the detritus produced by their disintegration which masks all the other structural parts. The greater portion of this detritus consists usually of oil-globules of the most diverse and, at times, considerable size. These form here and there groups and rows, which, by their configuration, suggest the idea of the hepatic cells and their net-work; usually, however, all trace of any regular arrangement is wanting. In other cases, occurring apparently less frequently, the detritus, as well as the contents of the surviving cells, consist chiefly of molecules which do not possess the optical and chemical characteristics of fat.[1] Within the separate cells, as also between the products of the disintegration, there are found, in greater or less amount, granules and flakes of yellow or green coloring matter, which are at times especially numerous in the vicinity of the central veins. Finally, the detritus often contains crystals of bilirubin; at times, also, such crystals are met with in the hepatic cells (Schueppel [in Burkart], Lewitski and Brodowski).

In cases of the second group, the atrophic liver exhibits, as has already been stated, alternately red and yellow portions, in consequence of which it looks as if composed of two different substances.[2] As regards the relative amount of space occupied by the two substances, there exists the greatest variety. At times the red substance constitutes the bulk of the mass, the yellow masses, the circumference of which varies from that of a lentil to that of an apple, being scattered therein in the form of islets, or (Klob, Waldeyer, Perls) grouped like foliage around the larger ramifications of the portal vein; the left lobe then consists

[1] It is supposed by some that even the interstitial tissue is transformed into granular and fatty detritus; in reality, however, there exists only a decided filling-up of the secretory canals with the reabsorbed detritus of the hepatic cells.

[2] For illustrations vide *Riess*, Charité-Annalen, Bd. 12, H. 2, Taf. 2, Fig. 5; *Waldeyer*, Virch. Arch., Bd. 43, Taf. 16, Fig. 4; *Zenker*, Deutsches Arch. f. klin. Med., Bd. 10, Taf. 4.

occasionally exclusively of red substance; in exceptional cases this is found to a greater extent on the left margin of the organ.[1] At other times the yellow portions predominate, and enclose, here and there, larger or smaller irregularly defined red portions, which at times are evidently located about the ramifications of the hepatic veins (Zenker). The least frequent arrangement is that in which the separate acinus contains red substance in the periphery and yellow in the centre, or *vice versa*. Usually the two varieties of substance may be recognized even on the outer surface of the organ; this presents a spotted yellow and purplish-red look, appearing prominent at the yellow points and depressed at the red; this dissimilarity is still more distinctly manifested, however, at the cut surfaces. The red portions, the color of which sometimes inclines more to gray, at other times to violet or brown, are considerably collapsed, of a flabby, more rarely of a firm, consistence, and extremely tough, occasionally almost like leather; their cut surface is smooth, and either entirely homogeneous (Zenker), or it may exhibit extremely small acini separated from one another by distinct lines (Riess, Klebs, Perls). The yellow portions, on the other hand, possess, as regards their appearance and consistence, precisely the same character as the hepatic parenchyma in the cases of the first group; where they border on the red substance, they project more or less beyond the line of the latter, in consequence of which the circumscribed yellow islets often look like tumors seated in the red substance. Moreover, the microscopic character of the yellow portions is, as a rule, precisely the same as was ascribed above to the yellow-softened liver; at times, however (Klob, Rosenstein, Waldeyer, Klebs, Zenker), the hepatic cells contained within them are for the most part still preserved, and, being filled with a finely granular, albuminous or fatty mass, are enlarged. In the red portions, on the other hand, the hepatic cells are completely wanting, or they are found, at most, isolated and manifestly on the point of disintegration (Riess, Waldeyer, Perls). There is usually seen merely a pale connective tissue, in

[1] Examples of this unusual condition will be found in the case communicated by *Rehn* and *Perls*, and in the two cases of *Standthartner*.

some parts homogeneous, in other parts striated or fibrous, and within this a slight collection of fat globules mostly quite minute, a few bile-pigment granules and isolated bilirubin-crystals. According to an observation of Klebs, there appear at scattered points, and chiefly, as would appear, at the line of boundary of the former acini, aggregations of lymphatic round cells, which lie in the dilated interspaces of the interstitial tissue. In many cases (Klob, Rokitansky, Riess, Gayda, Waldeyer, Zenker, Degen, and others) the connective tissue in the vicinity of the finest ramifications of the portal vein and of the peripheral capillaries of the acini is found to be studded with numerous roundish and oval granules, which in all probability originated in a recent proliferation supervening during the course of the atrophy.

This view derives especial support from the abrupt cessation of the granular development at the margin of the still surviving lobules in the yellow portions, which is particularly dwelt upon by Waldeyer in his case. Klob found (1865), likewise, in the jaundiced softened portions, merely a very firm connective tissue with single elongated nuclei; in the dark-red substance, on the other hand, a considerable proliferation of the nuclei proceeding from the inter-acinous tissue and from the adventitia of the vessels. In the cases of Riess, also, where the development was found in both substances, it was, nevertheless, much further advanced in the red.

Another constituent of the red substance, described by Waldeyer, Klebs, Zenker, Winiwarter, Perls, A. Thierfelder, and Cornil, consists of peculiar rows of cells[1] resembling glandular tubes, within which, according to the view of Waldeyer, Zenker, and Winiwarter, an outgrowth of new hepatic parenchyma seems to take place proceeding from the minute gall-ducts that remain preserved; though it is thought more probable by Klebs and Perls, that surviving columns of hepatic cells form this kind of capillary-ducts.

Both of the conditions above pictured of acute atrophied liver, of which one is characterized by a uniformly *yellow* color, and the other by the presence of *yellow* and *red* portions, are re-

[1] Engravings may be found in *Kiebs*, Handb. d. path. Anat., S. 149, Figs. 32 and 33; *Zenker*, Deutsches Arch. f. klin. Med., Bd. 10, Taf. 3, Figs. 4 and 5; *A. Thierfelder*, Atlas d. pathol. Histol., Taf. 17, Fig. 7; *Cornil* et *Ranvier*, Manuel d'anat. patholog., p. 890, sqq.

garded by Klebs as the product of two different processes, designated by him as yellow and red atrophy. Zenker, Rokitansky, and Perls, on the other hand, regard the red atrophy as merely a subsequent stage of the yellow, which is never completely developed throughout the whole organ, but only in isolated divisions, sometimes larger, sometimes smaller; whereas, in the remaining portions, the process only reaches that stage which is indicated by the yellow atrophy, either having begun at these points at a later period, or having developed more slowly. In support of this theory, Zenker has produced convincing arguments, principally from a pathologico-anatomical standpoint; and, as will be shown hereafter, clinical facts point to the same conclusion.

As a circumstance which seems opposed to the idea of the further development of the yellow into red atrophy, importance is attached by Klebs to the sharp line of demarcation between the two substances. According to the observations of Zenker, however, this line is by no means always microscopically perceptible, and the microscopic examination reveals at the margin of both substances most distinct stages of transition. This view harmonizes with the statements of other authors. Thus Paulicki remarks of the saffron-yellow islets, which in his case were found scattered in the partly brown and partly red hepatic parenchyma, that they were sometimes sharply circumscribed, but at other times they merged gradually into the latter variety. Perls observed, upon microscopic examination of a fresh liver, as well as of a specimen hardened in Mueller's fluid and alcohol, the very gradual merging of the yellow into the red zones.

Whether those cases are the most numerous in which the liver presents a uniformly yellow color even in well-marked general atrophy, or whether those other cases form the larger number, in which, in portions of the gland varying in extent, the process has already progressed to red atrophy, cannot be accurately determined from the statistical material hitherto collated.

Of the 143 Observations here utilized there are 37 which are without doubt, and 19 which are probably, to be referred to the latter category; whether, however, the remaining 87 belong altogether to the former class appears, at least, very questionable, the description of the liver in many of them not being sufficiently accurate to enable us to determine therefrom with any certainty as to the existence of red atrophied portions, these having been undoubtedly often overlooked, especially when of but slight extent, or incorrectly interpreted (termed, for instance, extravasations of blood). The relatively great frequency of the highest grade of

atrophy, characterized by the red, firm spots, is very plainly indicated by the circumstance that Zenker, who first of all recognized the nature of these spots, found them very distinctly portrayed in at least ten of the twelve cases which he had the opportunity of examining.

A deviation from the condition of the liver above described is often met with, in so far that its volume and weight are only in slight degree (for instance, the former only in thickness) or even not at all reduced below the normal point, although the high grade of granular degeneration and the very great disintegration of the hepatic cells leave no doubt as to the existence of the process in question. In the majority of these cases the explanation lies in the circumstance that the process has been developed in a liver which, by the over-distention of its glandular cells with fat, or by the proliferation of its interstitial tissue, had become enlarged, and on this account was not reduced to so small a volume by the acute atrophy as would result in an organ previously of normal size.

Thus, in a case of Liebermeister, for instance (l. c., S. 185, Beob. 39), the fatty liver of a toper, thirty-seven years of age, was enlarged in its superficial area, but only 2¼″ thick in the right lobe, 1″ in the left, and 1,520 grammes in weight. Frerichs describes (l. c., Bd. 2, S. 11) the liver of a toper, thirty-six years of age, who had died of acute atrophy, in which the connective-tissue stroma was considerably thickened; in the right lobe it was 13″ broad and 3″ thick, and weighed 2,100 grammes.

In certain rare cases the slight grade of reduction in size is due to the circumstance that death has supervened just as more advanced changes in a portion of the liver had begun to set in.

To this class of cases belong, for instance, that reported by Frerichs (l. c., Bd. 2, S. 16) and one reported by Winiwarter, to be referred to more particularly hereafter.

The smallest *bile-ducts* appear, as a rule, to remain preserved, and, as already stated on page 254, in the red-atrophied parts they seem not unfrequently to increase by proliferation. Occasionally they enclose masses of bile-pigment ramifying in the shape of vessels. Bollinger found their epithelium in a state of fatty degeneration; by Perls they were observed to be in part abnormally crowded with epithelium. The remaining bile-ducts located

within the liver are most commonly quite empty, presenting nothing abnormal upon their inner surface; less frequently catarrhal changes are exhibited by the mucous membrane. A similar appearance is presented by the large excretory ducts; as a general rule, they are empty, and the duodenal orifice of the ductus choledochus is unobstructed. Yet the mucous membrane is not unfrequently swollen in the *pars intestinalis* (Paulicki, Schultzen, and Riess), or its tube is occluded by a plug of mucus (Bamberger, Mann, Rosenstein, Davidson, Waldeyer, Schultzen and Riess, Rehn and Perls, Fick). In such cases the mucous contents are often scattered over the entire choledochus as well as over the cysticus and hepaticus, whereas, at other times, these canals even are free from catarrh and collapsed, or they may contain a little yellowish or brownish fluid. Occasionally the mucous membrane of the ductus choledochus immediately above the plug exhibits a strong yellow tinge. In Waldeyer's case this condition existed also in the cysticus, whereas the ductus hepatici were quite pale.

The *gall-bladder* is usually relaxed, and at times empty; it commonly contains, however, a mucous fluid, which often looks colorless and gray, but more frequently green or yellow in various shades. In a case of Frerichs (l. c., Bd. 2, Beob. 3), and in that of Sander, notwithstanding the bilious coloration, no bilirubin could be detected. It is only occasionally, in cases running a very rapid course, that the contents of the bladder do not vary perceptibly from the bile ordinarily found in the cadaver.

The *blood-vessels* of the liver present no abnormities appreciable to the naked eye. Upon examination with the microscope, Liebermeister found in one case (l. c., S. 187) the walls of the ramifications of the portal vein in a state of fatty degeneration. The blood contained in the large vessels is thin. Extravasations of blood occur but seldom, and then in but slight degree. No positive evidence has been afforded of any hyperæmia of the capillaries in the less-altered portions of the organ. The red border around the acini, which Frerichs in one of his cases (Bd. 1, Beob. 15, S. 215) regarded as a congestion of the ramifications of the portal vein, was, in all probability, as suggested by Klebs and Zenker, substance that had undergone red atrophy. Upon

artificial injection (from the portal vein and hepatic vein) the capillary net-work can be but very imperfectly filled, the injected material being extravasated between the hepatic cells (Frerichs, Demme, Riess). At times the *lymphatic glands of the porta hepatica* are swollen.

In the parenchyma of the liver, especially upon the outside and upon the cut surfaces when exposed to the air, as well as upon the inner surface of the hepatic veins and the ramifications of the portal vein, are frequently formed crystalline deposits of *leucin* and *tyrosin*, to which attention was first of all directed by Frerichs (1854); these are frequently observed in very considerable quantity,[1] which is increased as evaporation progresses. Under the microscope they appear as balls and globules, which frequently exhibit radiated or concentric stripes, and as fine needles grouped together like sheaves or husks.[2]

Of the thirty-four cases containing statements respecting the presence of these substances in the liver, in fourteen instances both were found; in six cases, leucin alone; in four, tyrosin alone; and in twelve, neither of the two.

The quantity of *fat* (ethereal extract) contained in the acute atrophied liver amounts, as has been ascertained by two analyses communicated by Perls,[3] to two- and threefold that of the normal average; the remaining solid substance of the organ undergoes a corresponding reduction; the quantity of water is, however, not diminished.

As to the presence of *sugar*, the watery extract of the liver was examined by Oppolzer and Liebermeister with negative results.

Bacteria have been recently discovered by some observers in the acute atrophied liver.

Klebs has observed once, according to his own report,[4] and several times, as would follow from a statement of Eppinger, very large accumulations of bacteria.

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[1] Occasionally the deposit does not begin until a considerable period after the autopsy (*Foerster*, *Mann*, *Lewitski*, u. *Brodowski*).

[2] For illustrations, vide *Frerichs*, Atlas. Heft. 1. Taf. 2.

[3] Centralbl. f. d. medic. Wissensch., 1873, S. 802; Berl. klin. Wochenschr., 1875, S. 651.

[4] Tagebl. d. Vers. d. Naturf. zu Leipzig. 1872. S. 223.

In one of the cases examined by Klebs, and in two other cases besides, Eppinger succeeded in demonstrating the presence of bacteria and micrococci in the large and small gall-ducts, as well as in the interstitial connective tissue; and in one of these cases he found even the hepatic cells and gall-duct epithelium of the yellow portion, that were still tolerably preserved, impregnated with microspores. In all these cases it is highly probable that bacteria, proceeding from the intestines, have penetrated into the gall-ducts, and, at points, still further into the parenchyma of the liver. In two other observations the bacteria were unquestionably a post-mortem formation: in those of Waldeyer their presence was confined to small blue-black spots (pseudo-melanosis from sulphate of iron) in those portions of the organ completely atrophied; in the case of Zander they appear, indeed, to have been present at all points in the liver, which was throughout colored yellow; but the autopsy was not performed until fifty-eight hours after death.[1]

In the above account of the alterations presented by the liver in acute atrophy, two of the most recent Observations have not been made use of; because they differ so considerably from all others as regards the histological appearances, that they seem to demand special mention.

In a case running a very rapid course, where only the left lobe was materially reduced in size, Winiwarter observed at certain points of the right lobe—whose structure was still well preserved—a considerable extension of the interstitial tissue as well in the circumference as within acini, due to an abundant deposit of lymphoid cells, and to a new-growth of fibrillæ and spindle-form connective-tissue corpuscles; and even in the hepatic cells he found, in addition to the nucleus, smaller bodies which he regarded as wandering lymphoid cells. According to the representation of this observer, along with the increasing proliferation of the round cells and the connective tissue, the regular arrangement of the hepatic cells becomes lost; these grow smaller, appear as if eroded, and finally break up into detritus. The emigration of white blood-corpuscles, and the formation of new connective tissue in the vicinity of the vessels, is dwelt upon also by Frerichs, in a case reported by him from the clinique of Gerhardt. In the case related by Lewitski and Brodowski there existed, likewise, an infiltration of the interstitial connective tissue with small cells. Moreover, in those parts of the parenchyma that have not yet undergone disintegration the acini were enlarged, and the glandular cells three or four times smaller than normal; but their number was still considerably increased, while their protoplasm was, for the most part, highly granular, and contained oil-globules. From these appearances it was concluded by the observers that, in the beginning of the process, there takes place, in addition to the emigration of the

[1] The case communicated by *Dupré*, where the presence of a very large number of micrococci was demonstrated by *v. Recklinghausen*, is, in reality, one of alterations in the liver, the result of acute puerperal septicæmia.

colorless blood-corpuscles, a proliferation of the hepatic cells, and that the new cells undergo fatty degeneration. They maintain, moreover, that there exists a proliferation not only of the finest gall-ducts, but also of the intra-lobular blood capillaries. The red portion of the liver consisted chiefly of very thin-walled coils of capillaries greatly distended with blood, whose calibre was, for the most part, narrower than that of the ordinary intra-lobular capillaries.

As respects, now, the lesions in the remaining organs, there is almost invariably present a universal *icterus*, sometimes of a higher, at other times of a lower degree. In the kidneys the convoluted tubules are occasionally crowded to distention with crystalline gall-pigment (Buhl, Paulicki). The large intestine contains, as a general rule, gray or grayish white, clay-colored, less frequently grayish yellow, loamy fæces ; but in addition to this, bile is found by no means rarely in the upper portion of the small intestine, often in considerable quantity, usually, however, only enough to tinge the mucous membrane or its slimy coating (Bright, Bamberger, Foerster, Riess, Waldeyer, Degen, Fick, and others).

Still other organs, in addition to the liver, are also found in a condition of granular disintegration. Indeed, fatty degeneration more or less advanced, of the *epithelium of the kidneys*, and of the *muscular tissue of the heart* appears to be uniformly present, this lesion having been found in all cases, when particularly looked for,[1] and in many of the remaining cases the statements respecting the macroscopic character of these parts leave but slight doubts as to its presence. Upon the other hand, in the *musculature of the body* it has thus far been demonstrated in but few cases (one by Paulicki, one by E. Wagner, three by Schultzen and Riess), and in one case in the peptic glands and epithelium of the mucous membrane of the stomach, in the vessels of the villi of the small intestine, as well as in the epithelium of the bronchi and of the pulmonary alveoli (Bollinger).

The *mucous membrane of the digestive canal* often presents catarrhal changes. At times the solitary and agminated follicles,

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[1] It is only in one observation, reported by *Trousseau*, that the kidneys, and in one related by *Morand*, that the muscular tissue of the heart, are said to have been normal, even upon microscopic examination.

as well as the mesenteric glands, are moderately swollen (Horaczek, Buhl, Waldeyer, Paulicki).

The *spleen* exhibits in more than two-thirds of all cases the signs of acute tumefaction, similar to that observed in acute infectious diseases; its volume may thus be augmented twofold, while the consistence of the pulp may be either diminished or increased, according as the course of the disease has been more rapid or protracted. In the remaining cases, the spleen is either of usual size or even smaller than usual. The absence of the swelling of the spleen may commonly be attributed to hemorrhage from the roots of the portal vein. It not unfrequently happens, however, that even after such a hemorrhage, the organ is still enlarged but at the same time pale and flabby. In many instances the swelling appears to be prevented by thickening of the splenic capsule.

The *blood* is dark, and, as a rule, thin. In the heart and large vessels, the coagula, if present at all, are loose; firm separations, like the rind of bacon, are quite rare. Other anomalies of the blood are by no means sufficiently constant to be considered as essential concomitants of the disease. In a few cases (Buhl, Bamberger) the white corpuscles were increased. The presence of leucin and tyrosin has been more frequently demonstrated in the blood of the heart and venæ cavæ, and in some instances, also, in still other localities outside the liver, as in the blood of the axillary vessels, in the spleen, brain, and kidneys (Frerichs, Pleischl, Oppolzer, Bamberger, Vallin). In one of Frerichs' cases (Klinik, Bd. 1, Beob. 16) the blood contained urea in "quite a considerable quantity;" though in another case of the same author (ibid., Bd. 2, Beob. 1) none was found, and in three cases occurring in Oppolzer's clinique but very little.

Extravasations of blood occur in at least three-fourths of all cases, and commonly in several, often in very numerous portions of the body. Most frequently the contents of the stomach and intestine are found to be bloody, and ecchymoses are observed in the subserous structure of the peritoneum, the epicardium, and pleura; these are seen, furthermore, in the mediastinal, retroperitoneal and intermuscular connective tissue, in and beneath the outer skin, in the mucous membrane of the stomach, the pel-

vis of the kidneys and the bladder, in the muscular tissue of the heart and beneath the endocardium, in the lungs and in the cortical substance of the kidneys; they are most rarely encountered in the brain (Breithaupt, Oppolzer, Rosenstein) and in the meninges (Tuengel). In somewhat more than a fifth part of the cases they are limited to the parts from which the portal vein draws its supply of blood.

The *brain* appears for the most part normal. It frequently presents the characteristics of anæmia or of venous hyperæmia, and still more frequently the alterations due to œdema and hydrocephalic softening.[1]

In the *lungs* are frequently found hypostatic hyperæmia and œdema; hepatization, on the other hand, is quite rarely seen, affecting usually, when present, the right lower lobe.

Serous transudations in the peritoneal cavity are occasionally met with in cases where the process has advanced in large sections of the liver to red atrophy. The color is either purely icteric or, in consequence of an admixture of blood, dirty red; the quantity is usually slight; it is only in cases running a comparatively slow course that it is at times more considerable (6–8 litres, for instance, in Waldeyer's case), and there are then commonly present in the other serous cavities, as well as beneath the skin, dropsical accumulations. In hemorrhagic infarctions of the lungs, a serous effusion may exist in the pleura alone (Zimerman).

Symptomatology.

The *hepatic dulness* exhibits in most cases a rapidly progressive *diminution*, both as respects its extent and its degree. This diminution begins regularly at the left lobe, in consequence of

[1] In a case of acute atrophy of the liver produced in all probability by phosphorus poisoning, Herzog *Carl*, of Bavaria (Virch. Arch., Bd. 69, S. 62), found in the cortical substances of the brain fatty degeneration of the ganglion-cells and of the intercellular substance, disruption of the latter into globular masses of 0.02–0.03 millimetres in diameter, which were disposed partly in coarsely granular and partly in concentric layers; furthermore, at certain points were seen entire rows of small tyrosin bundles, and in the capillary vessels large oil-drops (as in fat-embolus after the destruction of the bones of the extremities).

which the dull sound in the angle between the two arches of the ribs is replaced by a clear tympanitic sound. In the vicinity of the right lobe the dulness is diminished by the lower margin moving upward, while along the line of this margin, and for a space more or less extensive above it, it acquires a tympanitic resonance; this dulness at the anterior surface of the organ may ultimately disappear completely, in consequence of which in the axillary line the sound emitted by the lungs is separated from that of the bowels only by a narrow strip of dulness. This almost complete disappearance of hepatic dulness is attributable chiefly to the circumstance that the relaxed organ collapses backward, coils of intestines forcing their way into that anterior portion of the hypochondrium thereby rendered vacant.

We are justified, in a majority of cases, in regarding the diminution of dulness as evidence of a reduction in the volume of the liver, meteorismus being entirely absent, or at least not existing in such a degree as to account for the changes in the percussion-sounds in the hepatic region. It frequently happens that the abdominal walls are even very much relaxed, and we are thus enabled to force upward the points of the fingers unusually far behind the right arch of the ribs; more rarely we may under such circumstances succeed, at the beginning of the shrinking, in feeling, behind the arch of the ribs, the sharp margin of the organ that has sunk backward (Pleischl, Bamberger, Liebert, Rehn).

The reduction in size becomes, as a rule, first of all appreciable in the latter days of life. Restricting ourselves to such cases in which the conditions of the organ as respects its size had previously been made the subject of accurate observation, it is usually upon one of the last three days, and most frequently upon the day preceding the last, that this diminution is for the first time clearly made out.

At how late a period and, at the same time, how rapidly this reduction may take place, is indicated, among other things, by an observation of Davidson: twenty-three hours previous to death the hepatic dulness was perfectly normal, just as it had been twelve hours earlier; fourteen hours later it had diminished in the left papillary line to two centimetres, and in the left median line to three and one-half centimetres; while toward the left of the median line, beyond which it had extended by six centimetres, it was no longer distinguishable.

It not unfrequently happens, however, that the reduction in size is plainly marked as early as four or five days previous to death, and, indeed, examples are not wanting of a still earlier commencement.

Thus, in a case of Bamberger, the reduction in size was appreciable as early as twelve days previous to death, progressing in its subsequent course to an almost complete disappearance of the dulness. Similar observations have been reported by Guckelberger, Oppolzer, Demme, Paulicki, Erichsen, and Moxon.

At the stage when the diminution in the bulk of the liver is perceived, the cerebral symptoms are commonly already present, and it very frequently happens that these symptoms lead, first of all, to an exact determination of the area of dulness. The reduction in volume may frequently be made out, however, as early as one or two days before their appearance (Merbach, Sander, Sieveking, Rosenstein, Goodridge, Kowatsch).

In a number of cases, previous to the appearance of any appreciable reduction in volume, the liver has been found to be larger than normal. If those cases are excluded in which alcoholismus, syphilis, or some chronic affection of the heart might have played a part, there still remain nine instances (Bamberger, Sander, Mettenheimer, Merbach, Mann, Huppert, Sieveking, Burkart, Rehn) in which the increased volume cannot be regarded as resulting from some pre-existing or complicating affection, but must be referred to changes belonging to the early stage of the very process giving rise to the atrophy. The strongest proof of this fact is furnished by the observations communicated by Mann and Rehn: here the extent of hepatic dulness appeared, upon the first examination, normal; two days later, enlarged; and at the expiration of two days more, reduced below the normal size. Oppolzer[1] also observed in one instance that the liver was larger previous to the wasting. In the other cases reported the enlargement was present upon the occasion of the first examination, and no subsequent diminution in size was noticed.

There are unquestionable cases of acute atrophy in which the signs of diminution in the size of the organ are, up to the last,

[1] Wiener medic. Wochenschr. 1858. S. 474.

wanting. At times, especially in lying-in women, the disease takes on so rapid a course that it does not progress to any appreciable reduction in volume, from the fact that life becomes extinct before any very extensive resorption of the products of disintegration has occurred. Upon the other hand, even where the course is more protracted, the extent of dulness may remain normal, provided the degeneration and disappearance of the glandular cells is accompanied by hyperplasia of the interstitial structure, which prevents the collapse of the parenchyma (Riess). If the disorder be developed in a liver enlarged by chronic proliferation of connective tissue or by fatty infiltration, it may then, likewise, sometimes remain without any appreciable influence upon its volume. More frequently, however, the volume undergoes, under such circumstances, an evident reduction, even if it does not also, as a rule, fall below the normal size (Frerichs, Tuengel, Liebermeister, Boese).

Picot (Jour. de l'Anat. et de la Physiol., Vol. 8, No. 3) recounts a case where, in a woman affected with syphilis, the organ, enlarged by diffuse interstitial hepatitis, was reduced below the normal size within a period of two days. Upon post-mortem examination it was found to weigh but 750 grammes, and exhibited complete disintegration of the parenchyma-cells.

Painfulness in the region of the liver does not occur altogether so frequently as earlier accounts appear to indicate. According to Frerichs, this was met with in three-fourths of the thirty-one Observations made use of by him. In about one-third of the cases forming the basis of the present paper, no mention is made of this symptom. In almost a fifth of the remaining cases its absence is expressly noted. (It was found wanting by Bamberger in all of the six cases that had fallen under his observation up to the year 1856.) When this sensitiveness is present, it does not usually make its appearance until the commencement of, or during the course of, the second stage of the disease. Pressure in the region of the liver, as well as strong percussion, then calls forth active indications of pain, and often, even in coma, when pinching the skin and pricking with a needle are no longer followed by any reaction, it induces distortions of the face and defensive movements. Less frequently voluntary

complaints are made of severe pain in the region of the liver. Still, even in the first stage there occasionally exists an abnormal sensitiveness to pressure in this region, but more frequently a pain, usually merely of a dull character, at the epigastrium. The latter may possibly, with equal propriety, be referred to the gastric derangements as to the affection of the left lobe of the liver. But, furthermore, as regards the more decided indications of pain in the second stage, it appears, occasionally, questionable whether these are directly connected with the morbid processes within the gland. Many patients respond to pressure at other points of the abdomen, or even of the upper part of the body, in precisely the same manner as when pressure is applied in the hepatic region. As respects such cases, the statement of Bamberger is very probably correct—that we have here to deal with hyperæsthesia of the skin, rather than with painfulness of the liver. Occasionally, the region of the liver appears free from pain as long as the patient retains consciousness; and not until after this has disappeared, do those symptoms supervene upon examination, that are interpreted as indications of pain. Possibly, these phenomena are here merely the expression of an abnormally exalted reflex-excitability.

Of the *gastric symptoms* with which the disease begins, the *falling off in appetite* is the most constant, and in rare cases the only derangement. This may be slight even up to the second stage; more frequently, however, a decided anorexia exists even from the beginning. *Vomiting* occurs in the first stage in somewhat more than one-half of all patients, and in part of the remainder nausea, at least, is present. The vomiting sometimes makes its appearance at an early period—being frequently mentioned as first symptom of the disease—at other times not until during the course of the first stage; occasionally it occurs only once, but usually takes place repeatedly or very frequently, and then may be prolonged into the second stage. The substance vomited consists chiefly either of the ingesta, or, and indeed more frequently, of mucous liquid which, judging from its color and taste, contains by no means rarely (in nearly a quarter of the cases) bile. In the second stage vomiting is a more constant symptom; even in cases where it has not hitherto

existed, or has ceased for a considerable time previous, it is wont to introduce the severe cerebral symptoms. The evacuations, too, may be then of a mucous character, and, notwithstanding the severe icterus, even bilious; and this condition may be presented the day previous to death, and even upon the last day of life (Trousseau, Stockmayer, Erichsen, Mann); more frequently, however, the stools contain in the second stage admixtures of blood more or less altered, or they may consist altogether of this matter. The cases in which vomiting is absent during the entire course of the disease constitute—including under this category all where this symptom is not mentioned—about one-fourth of the entire number. The bowels are, as a rule, confined, and frequently obstinate constipation is present. Spontaneous diarrhœa is very rarely met with.

Icterus forms in the majority of cases (in about two-thirds) one of the earliest symptoms, appearing almost simultaneously with the gastric derangements, or at least but few days after the latter. In about one-fourth of the cases it does not supervene until from the fifth to the seventh day, and still less frequently not until after the lapse of two or more weeks. Where the malady runs a very rapid course, it sometimes does not make its appearance until the day previous to that of death, or until the last day, in consequence of which its outbreak is coincident with that of the severe brain symptoms (Lewin, Frerichs, Hugenberger, Homans, Chamberlain, Vallin), or it may even follow after the latter (Hanlon, Frerichs, Seidel, Mettenheimer). Apart from the cases of the latter variety, in which, owing simply to their short duration, no severe development of jaundice is commonly reached, this phenomenon generally attains a considerable intensity. The *skin* always becomes gradually a deep yellow, and finally saffron, orange, or even greenish. The urine presents, as a rule, Gmelin's reaction for bile-pigment. The severer the icterus, the better marked is usually this reaction. Where the jaundice continues very slight, and the urine retains its normal color, we may fail completely to obtain the reaction (as, for instance, in Observation 17 of Frerichs, l. c., Bd. 1, S. 222); occasionally, however, even in well-marked jaundice, it is not obtained, or is but faintly produced, although the dark color and the yel-

low foam of the urine lead us to infer the presence of bile-pigment (Trost, Riess). Many observers have succeeded in demonstrating the presence of biliary acids in the urine (F. Hoppe,[1] Huppert, Hugenberger, Wood, Davidson, Rosenstein, Kowatsch, Boese, Schultzen-Riess, Fick); the negative result, with which some others have tested for this substance, is to be explained, at least in part, by the insufficiency of the method resorted to. The *stools* are, as a rule, of a dirt- or clay-color, or almost completely colorless; but occasionally, even when the icterus is severe, there may ensue in the first stage, and now and then even in the second, alvine evacuations of normal color; it may also happen that the fæces, which elsewhere look gray, present at certain points a bilious coloration.

When pregnant women are attacked by the disease, whether the *fœtus*, too, becomes jaundiced depends upon the duration and degree of the icterus.

If the course of the first stage is protracted, there then occasionally occur fluctuations in the intensity of the icterus. Generally, however, this increases up to the last day of life. The assumption of Oppolzer, reported by Schnitzler,[2] that this increase ceases as soon as the wasting of the liver is distinguishable, is not, at least as respects the coloration of the skin, of general validity.

Compare, for example, the case of Bamberger in the Transactions of the Physico-Medical Society at Würzburg, Bd. 8. Yet, some observations tend indeed to show that ultimately the elimination of the bile-constituents by the kidneys again diminishes. According to the results obtained by Huppert from weighing the sodium salts of the biliary acids derived from the urine, which still contained an admixture of rather numerous foreign substances, the elimination of biliary acids in the case in question appeared to increase with the progress of the disease, but to appreciably diminish again shortly before the end. In a case narrated by Fraentzel, occurring in Traube's clinique, the urine contained less bile-pigment on the last day of life than on the preceding day, whereas the yellow coloration of the skin had become still more intense.

In exceptional cases the icterus may be altogether absent. The cases in which this was wanting are those characterized by

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[1] Virchow's Archiv. Bd. 13. [2] Deutsche Klinik. 1859. S. 286.

their unusually rapid course. The following, communicated by Bamberger,[1] affords an example.

In a primipara, thirty years of age, chloroform had been repeatedly administered during confinements, and after the extraction of a living child, on account of metrorrhagia, the placenta had been forcibly removed. Upon the next day great weakness, moderate fever, and sinking in of the face. Upon the morning of the following day, apart from the accelerated pulse (110), no morbid symptoms, but as early as 10 o'clock in the forenoon complaint of great distress, hiccough, severe thirst, cold hands and feet, and pulse almost imperceptible. During a bath the eyes were violently rolled, and the patient began to sing gay songs. After the lapse of a few hours, attacks of mania came on, with slight muscular twitchings. At midday death ensued, thirty-eight hours after delivery. No trace of icterus was present, either during life or upon the cadaver; and yet, the liver presented the most highly developed grade of acute atrophy, and the disintegration of the hepatic cells was so complete that their traces could here and there with difficulty be detected. Moreover, in a case reported by Liebermeister (l. c., S. 200, Beob. 45), where the disease was developed in a woman, aged thirty-five years, during the course of an acute peritonitis, no trace of icterus was discovered, either on the surface of the body or in any other organ (excepting the liver). Eppinger quotes a case of very far advanced acute atrophy of the liver in a patient convalescent from typhoid fever, and reports the appearances found at the autopsy as affording proof that *the icterus may be absent even when the course of the disease is unusually protracted;* but the account given by him of the history of the patient is in this case so meagre, that it cannot be determined whether the course of the hepatic affection was here in reality a protracted one.

An increase in the *splenic* dulness is frequently, though not invariably, present. It was observed in not quite two-thirds of the cases in which an examination was made with this point in view. As a rule, it is but slight, and attains, at most, to the extent of the palm of the hand. In exceptional cases the anterior point of the tumor can even be felt. Indications of pain upon percussion in the hepatic region, or upon palpation of the left hypochondrium, are occasionally observed, though we cannot in all instances conclude with certainty therefrom that the organ is swollen. As respects the date of the beginning of the splenic swelling most observations afford no clue. This lesion and the wasting of the liver are usually detected simultaneously; but it should here be observed that in many cases no accurate determi-

[1] Krankh. d. chylopoët. Syst. 2. Aufl. S. 522. Anm.

nation whatever of the size of this organ has been made previous to the appearance of the second stage. Yet a few observations are upon record (Pleischl, Chvostek, Demme, Oppolzer (1864), Traube, Davidson, and others) according to which the splenic tumor may be present as early as from one to six days before the reduction in the volume of the liver becomes recognizable, and in its further progress may still increase in size. The increase may occasionally continue as late as the last day of life. In case of severe hemorrhages in the region of the roots of the portal vein, the swelling may then rapidly again subside.

Hemorrhages are observed in more than one-half of all patients, and in almost one-half of the cases in which they occur they appear in more than one organ. Hæmatemesis is of the most frequent (in two-thirds) occurrence; according to the quantity of the effusion, a mass, resembling coffee-grounds or a blackish flocculent or tarry mass, is vomited; or else a dirty red fluid, or dark blood occasionally coagulated into lumps. In about one-fourth of the cases a discharge of blood, more or less altered, takes place from the rectum. There are, likewise, formed quite as frequently petechiæ and ecchymoses of the skin. Somewhat less frequently hemorrhages from the nose take place and still more rarely from the mucous membrane of the mouth. Occasionally, also, blood is contained in the urine, though usually in but slight quantity. In case of pregnant and lying-in women metrorrhagia often supervenes. In non-pregnant women discharges of blood from the genital organs are but seldom observed. Leech-bites are very apt to give rise to obstinate after-hemorrhages. By far the greatest number of hemorrhages occur in the second stage of the disease, and chiefly during the last two days of life; it is only in cases running a more protracted course that they occasionally begin some time—as early as nine days (Demme, Paulicki)—before the supervention of severe brain-symptoms.

As respects the *character of the blood* during the life of the patient, but very meagre accounts are to be found.

In a case reported by Horaczek the blood withdrawn by opening a vein upon the ninth day before death had not separated into clots and serum even after a lapse of several hours, but had only coagulated into a semi-firm friable mass.

Rosenstein, who examined the blood of his patient one-half day before death, found the colorless blood-corpuscles remarkably increased in number, the red corpuscles in part greatly shrivelled, and their stroma very rapidly becoming granular; in some red cells he was able to distinguish alterations of form (growth of processes, constrictions in the centre). A similar report is made by Fick with respect to two cases from the clinique of Gerhardt; in both, the color of the blood seemed more transparent than normal; the red corpuscles in the first case in part, and in the second throughout, presented an appearance as if their outer surface were covered with dots; the proportion of the white to the red corpuscles was in the first case as one to eleven; in the second normal. Schultzen and Riess demonstrated beyond doubt the presence of tyrosin in the liquid which they had expressed from the small blood-clots formed from the blood obtained by venesection four hours before death; leucin, on the other hand, was in vain sought for.

Fever is frequently present in the first stage of the disease. Among the anamnestic signs mention is not only frequently made, under the head of initial symptoms, of subjective febrile phenomena (chills and subsequent fever, usually in repeated attacks, increased thirst, exhaustion, etc.), but there are also reported, at least as regards the later period of this stage, records of temperature and pulse, derived from many cases, which correspond to a remittent fever of medium or low grade, such as is wont to accompany acute catarrhal affections. The *second stage*, on the other hand, is *at the outset uniformly free from fever*, as is commonly, also, the period immediately preceding the appearance of this stage: the temperature is either normal, or—what is of more frequent occurrence—is subnormal (between 37° C. [98.6° F.] and 36° C. [96.8° F.], often even as low as 35.5° C. [95.9° F.]), as is usually the case in icterus. In this respect it makes no difference whether the symptoms of irritation of the brain predominate or those of depression; the severest attacks of mania fail to exert any influence upon the temperature (Traube). Whereas in a portion of the cases the low temperature is maintained until death, or falls still lower (in a case of Fick it amounted seven hours before death to 35° C. [95° F.] in the rectum and 34.6° C. [94.3° F.] in the axilla), in others (in eighteen of the thirty-four cases collected by me in which a record was kept) an increase of temperature ensues toward the end of life. This does not begin until the last eighteen to thirty hours before death, and results frequently in only a moderate, but usually in

a considerable or even excessive elevation of the temperature. (In an observation of Wunderlich, for example, this amounted ultimately to 39.5° C. [103.1° F.]; in that of Traube, one-quarter hour before death, to 41.3° [106.3° F.]; in another of Wunderlich, at the time of death, to 42.6° C. [108.7° F.], and six minutes later, to 42.9° C. [109.2° F.].) In the second stage, likewise, the rate of the pulse is often, at the outset, abnormally low (between 60 and 40 to the minute), but at other times somewhat higher than would correspond to the existing degree of temperature. Not unfrequently it presents rapid oscillations independent of the course of the temperature. It varies chiefly from the latter, however, in that it constantly increases during the last days of life: in cases attended by final elevation of temperature it usually attains sooner than the latter a considerable height, reaching ultimately to 140–160; but even in those cases where the temperature continues subnormal until the end, the frequency of the pulse reaches to 120 and over. As respects its quality, the pulse presents occasionally at the beginning of the second stage no striking anomalies; more frequently, however, it is even at this period smaller and softer than normal. Toward the termination of life it becomes weak, and often even imperceptible.

The absence of fever in the beginning of the second stage may be regarded as a constant phenomenon. Among the entire number of observations compared by me are only two—one reported by Demme and one by Burkart—which seem to form an exception. The case of Burkart, in which the temperature was continuously elevated during the last three days (between 38° and 40.3° C. [100.4°–106.5° F.]), presents, however, in other respects not much that is anomalous, and if it belongs at all under the head of idiopathic acute atrophy of the liver, then death supervened in a very early stage of the disease, probably in consequence of the complication with double pneumonia. In Demme's case (l. c., Observation 1), in which the disease ran a very protracted course, a temperature of from 39° to 40° C. [102.2° to 104° F.] prevailed constantly throughout the last one and one-half weeks; but here, also, there existed, besides the acute atrophy of the liver, still other affections—namely, chronic nephritis and a left pleuritic exudation.

Upon the *skin* there appear in rare cases, besides the icterus and the extravasations, circumscribed hyperæmias, like those of roseola, or somewhat larger, which spread sometimes over the principal portions of the surface of the body, and at other times

are confined to the trunk or to the extremities. At times these make their appearance together with petechiæ, and are then probably only a precursor of the latter. Toward the termination of life, when the bodily temperature is subnormal, the skin is generally pale and less elastic; where, on the other hand, the temperature is increased, it is highly reddened and turgescent, especially in the face.

The *urine*, besides containing the constituents of bile, presents usually in many other respects an abnormal character. Toward the end of life its quantity falls more or less, and not unfrequently very considerably, below the normal average; it may amount, however, even on the day preceding that of death, to 1,400 c.ctm., and on the last day to nearly 1,000 c.ctm.

In a case reported by Fick from Gerhardt's clinique, as much as 3,000 c.ctms. were voided during the last twenty-four hours.

The specific gravity is, as a rule, above the average height (usually between 1,016 and 1,030).

In Observation 1 of Traube, on the day preceding death it was 1,010; in the case of Fick, just referred to, it was also 1,010 on the last day; in a case examined by Zuntz (*vide* Boese, l. c.), 1,036 on the last day.

The peculiarities of the urine characteristic of the disease are connected, however, with its chemical composition; it contains, in the majority of cases, considerable quantities of *leucin* and *tyrosin;* whereas the *urea* is remarkably diminished, traces only being often ultimately present, or it may even be no longer possible to detect this substance. Frequently, even upon allowing the urine to cool, though more often not until after evaporation and concentration, tyrosin is deposited in the form of delicate needles, which are grouped together in almost colorless bundles like sheaves, or in globular masses tinged with bile-pigment. Leucin, on the other hand, never makes its appearance as a constituent of a spontaneous urinary sediment; the concentrically striated, and in part finely spiculated globular masses, in which this substance is crystallized in its impure state, are not unfrequently found, however, along with the tyrosin needles in the residuum after evaporation of fresh urine; whereas, at other

times, it is only obtained by the repeated treatment of the evaporated urine with alcohol.[1]

Frerichs, to whom we are indebted for our knowledge of the occurrence of these two substances in the urine in acute atrophy of the liver, discovered them in all cases in which he looked for them. In addition to the cases communicated by him, the material here collated embraces thirty-four others (which constitute fully one-third of the observations published since the announcement of Frerichs' discovery) in which the urine was examined in this respect; in seven of these (Tuengel, Erichsen, Hugenberger, Riess, Baader and Winiwarter, Steiner, Rehn) the result was negative; in seventeen both substances were present; in three, the presence of tyrosin only is reported; in seven, leucin alone was found. It must be admitted, however, that the examination has not in all cases been conducted in a sufficiently reliable manner. This statement is particularly applicable as respects leucin, whose presence or absence has been inferred by some, merely from the result of the microscopic examination of the evaporated and concentrated urine. Nevertheless, the number of the perfectly authentic observations is large enough to admit of no doubt that in acute atrophy of the liver these substances, as a rule, and generally both, though less frequently but one of them, are contained in the urine, but that they also are wanting in many cases otherwise perfectly characteristic. Among the latter class are comprised those running a more protracted course, as well as those that are quite acute. At what period of the disease the substances in question first appear in the urine is not as yet ascertained, as they have hitherto been invariably first sought for during the second stage. Demme alone succeeded, in a case running a very protracted course (l. c., Observation 1), in demonstrating in the urinary sediment, as early as a month previous to death, small masses of tyrosin as well as leucin-globules.

Along with leucin and tyrosin, still other abnormal constituents of the urine, produced from albuminoid substances, are occasionally detected; thus, Frerichs discovered in one case (l. c., Bd. 1, S. 217) a substance similar to tyrosin and crystallizing in like manner, "but which differed in being more soluble and in containing a larger proportion of nitrogenous matter (8.83 per. cent.)"; by the same observer creatin was found in three cases (l. c., Bd. 2., S. 14, 16, 17) in large quantity; in three cases, coming under observation within the period of three months, Schult-

[1] As a general rule, it is sufficient to allow a drop of urine to evaporate upon an object-glass (it is better to add a little acetic acid to produce a decomposition of the uric acid salts), in order to obtain leucin and tyrosin in characteristic forms. For the chemical methods and reagents which are to be applied in doubtful cases for the eduction and diagnosis of this substance, *vide Neubauer* and *Vogel*, Anl. zur qualit. u. quantit. Analyse des Harns. 7. Aufl. 1876. S. 113 ff.

zen and Riess (l. c.; S. 74, 80, 85) found oxymandel acid and small quantities of sarco-lactic acid. The last-named observers discovered, moreover, in the urine in these two cases a substance resembling peptone (l. c., S. 72, 80), and, as was likewise detected by Frerichs, considerable extractive matter soluble in alcohol.[1]

The diminution of the *urea* in the urine, progressing frequently until it is completely absent, to which attention was, likewise, first directed by Frerichs, occurred in fourteen of the twenty cases in which the urine was examined by subsequent observers with reference to the presence of this substance. In the six remaining cases (Bamberger, Standthartner, Huppert, Rosenstein, Valenta, Fick) the quantity of urea excreted during the last days of life appeared, on the other hand, to be either undiminished, or even larger than normal. Still, these results, as has been justly urged by Schultzen and Riess, are untrustworthy, for the reason that the determination was made according to the volumetric method of Liebig, by which the peptonoid substances and much foreign matter contained in the alcoholic extract of the urine is at the same time precipitated by the action of the oxide of mercury. In one of the observations of Frerichs (l. c., Bd. 1, S. 216) phosphate of lime was also wanting in the urine. The quantity of chloride of sodium was very slight during the last days of life in all cases in which it was estimated (with the exception of one reported by Pleischl and Folwarczny).

Albumen is not unfrequently contained in the urine, still its quantity is generally slight.

It was found in nineteen out of forty-three cases in which the test for it was applied; in three cases only is the quantity of albumen stated to be considerable.

When the urine is allowed to stand, there is often formed a dry, yellow or greenish yellow, and often a dirty whitish *sediment*. This consists most frequently of epithelium from the urinary passages and the kidneys, which is usually tinged with bile-pigment, and filled with dull or glistening granules. In addition to this, it also contains, at times, masses of tyrosin. Less frequently the sediment consists exclusively of the latter. There is also found now and then a brick-red sediment, in which the urates are mixed with epithelium from the urinary organs, or

[1] In a case examined by *Zuntz* (*vide* Boese, l. c., S. 25), when the urine, that had been strongly concentrated and mixed with an equal quantity of alcohol, had stood for three days in a temperature of 0° C. [33.8° F.], crystals were deposited in the form of small plates and scales, perfectly analogous to those obtained by *Liebig* while engaged in producing inosic acid from the muscle of fowls.

with tyrosin crystals. Casts in the urine are described by but few observers.

The derangements on the part of the *nervous system* begin, as a rule, with symptoms which fail to indicate to a full extent the severity of the condition. These consist most frequently of violent headache, insomnia, restlessness, a gloomy, irritable temper; or, on the other hand, somnolence, great prostration, suppressed voice, and apathy. Less frequently there is observed palpitation of the heart with intensification of the heart-beat and of the first sound over the left ventricle, anxiety, abnormal sensitiveness to light and noise, fainting, hesitating speech. The duration of these initiatory symptoms varies from several days to a few hours. Occasionally they subside, and for a short time a better condition supervenes; they are usually followed, however, by the severe manifestations. Still, where the disease runs a very acute course, the appearance of the latter may also be without previous warning.

Of these severe manifestations the most characteristic are due to derangements of the psychical functions; they consist of *delirium* and a *state of insensibility.* The delirium is usually of a raging character, manifesting itself in the form of dancing about, violent temper, garrulity, loud singing, penetrating shrieks, anxious expression of countenance, attempts to escape, and the like. In at least one-third of the cases the excitement amounts at times to regular maniacal paroxysms. Quiet, wandering delirium occurs far less frequently. In about one-fifth of the patients, however, the delirium appears to be altogether absent. The insensibility, on the other hand, which, as a rule, runs through the various grades from slight stupor and somnolence to profound sopor and complete coma, is almost invariably present. It is only when the course is peracute—especially when hastened by hemorrhages, and, on the other hand, where it is very much protracted—that in quite isolated cases consciousness continues to be preserved until the last. (Stehberger, Beob. 2; Buhl, Waldeyer.)

With the derangement of the psychical functions are associated, as a rule, still other symptoms of irritation and paralysis of the central nervous system.

Convulsions make their appearance in adults in about one-third of the cases; in patients, however, who are still in early childhood, they are almost invariably found. There is observed most frequently slight or severe twitchings of certain groups of muscles, chiefly in the face, on the neck, extremities, often only on half of the body; almost as frequently there occur severe general convulsions; occasionally a muscular tremor extending over the entire body; furthermore, hiccough and grating of the teeth. With the clonic convulsions there is occasionally associated trismus; this is seen but seldom alone; tetanus is of somewhat more frequent occurrence.

Vomiting, too, possesses, especially in the second stage, the significance of a cerebral symptom. In a portion of the cases it generally makes its first appearance at the beginning of this stage; in other instances, where it was present even at the outset of the disease, but had subsequently ceased, it reappears at this period. Although it may be excited in part by the effusion of blood in the stomach, still the quantity of blood contained in the vomited matter is more frequently too slight to produce this effect.

There is occasionally found, where the temperature of the body is normal, a very active *thirst*, which cannot always be referred to the great loss of water consequent upon copious hemorrhages or frequent vomiting.

The *pupils* present generally an abnormal condition. They are usually dilated, and their sensitiveness to light is either diminished or intensified; at times, notwithstanding the dilatation, they are observed to react well. They are very seldom contracted. Traube (*vide* Fraentzel, Observation 1) found them, on the day previous to death, dilated and very slow to react; while upon the last day they were contracted and without reaction.

The *respiration* is often changed during the coma. In many cases the breathing becomes sighing, while short, deep, and generally noiseless inspiration is followed by an expiration which, at the outset, is rapid, but subsequently quite slow. More frequently it is snoring or stertorous. Irregular and intermittent breathing is also occasionally observed. Toward the end of life the number of respirations increases, and, in cases where the

temperature is normal, may rise to forty in the minute, and, with a higher temperature, to fifty and over.

To the symptoms of paralysis of the central nervous apparatus belong furthermore—first, those which are of more frequent occurrence: obstinate constipation, ischuria, involuntary evacuation of the bladder and rectum; second, those which appear in but few instances toward the end of life: severe meteorismus and profuse sweats. Finally, an analogous symptom, also, is the fuliginous deposit with which the lips, teeth, and tongue are wont to be coated in the course of the second stage.

Anomalies of *sensibility* are not, as a rule, to be observed, if we except the derangement of the perceptive faculties attributable to the high degree of stupor. In isolated cases only does there exist a more or less extensive hyperæsthesia of the skin, which may become quickly replaced by anæsthesia.

The order in which the various symptoms proceeding from the nervous system make their appearance is by no means a uniform one. Although at the outset the indications of irritation, and later of weakening and paralysis of the functions generally predominate, still both sets of symptoms usually run their course side by side, and are respectively interrupted in the most varied manner. Somnolence and delirium often appear simultaneously; or, at other times, the patient is already in an almost soporific condition before he begins to be delirious. Again, the severity of the disturbance that supervenes in the form of paroxysms may increase with the progressing loss of consciousness, and it may be shortly before death even that the delirium first becomes raging. Spasms hardly ever occur at the beginning of the nervous stage; a few patients die in convulsions. Vomiting, moreover, recurs in many cases—though not induced by gastrorrhagia—up to the termination of life. Now and then every indication of irritation is absent; at the most, headache and vomiting precede the sopor, which, without the supervention of delirium or cramps, becoming deeper and deeper, rapidly induces death. The symptoms of cerebral paralysis do not present, however, in all cases, a constant increase. Even when they have already attained a considerable height, they may again subside, in consequence of which the lost consciousness partially or—which is of

very rare occurrence—completely returns. Still, the persistence of other brain-symptoms—for instance, the abnormal dilatation and inactivity of the pupils—usually betrays even then the danger of the condition, and after a few hours, or often not until the lapse of twenty-four or thirty-six hours, the patient sinks anew into a state of insensibility. In cases where pregnant women are affected, such a temporary improvement not unfrequently ensues directly after confinement.

The impairment of the *general nutrition* is, as a rule, but slightly observable, owing to the short duration of most cases. It is only when the disease attacks individuals whose nutritive force has already suffered from other influences, or when it assumes a more protracted course, that any remarkable emaciation can supervene. (In a case of Wunderlich the bodily weight diminished by nearly three pounds within eight days.) Under such circumstances indications even of *dropsy* are occasionally developed, limited generally to slight œdema of the feet; in extremely rare cases only do transudations into the serous cavities take place, which are distinguishable during life.

Analysis of the prominent Symptoms of the Disease.

The *reduction in the extent of liver-dulness* is quite as much the result of relaxation as of the diminution of the volume of the organ, both of which conditions are produced by the disintegration of the hepatic cells and the resorption of the detritus. The previous enlargement of the liver that is occasionally observed, is in all probability due to the cloudy swelling of the secreting-cells that takes place at the commencement of the granular degeneration; that hyperæmia may form the precursor of the process, has at least not yet been demonstrated.

Indications of pain in the hepatic region are the more difficult to definitely explain, inasmuch as they are a very inconstant symptom. It is possible that the rapid collapse of the organ—as analogously in other affections its rapid swelling—exercises a mechanical irritation upon the nerve-fibres of the parenchyma, and, above all, of the serous coating; it is possible, too,

that the nerve-fibres are even implicated in the acute derangement of nutrition.

The mode of origin of the *icterus*, notwithstanding numerous attempts at explanation, has not yet been satisfactorily determined. The theory maintained, especially by English authors (Alison, Bright, Budd, Harley), and by Liebermeister—according to which the icterus is produced by the retention in the blood of the constituents of the bile, or of the substances intended for their formation, when, after the destruction of the gland-cells, the secretion in the liver ceases—harmonizes too imperfectly with the current notions as to the formation of the specific ingredients of the bile to justify its acceptance. Furthermore, this explanation would not suffice for those comparatively frequent cases in which the icterus makes its appearance as early as several weeks previous to death; that is to say at a period when, surely, no very extensive destruction of the hepatic parenchyma can as yet have taken place. The assumption of Rindfleisch,[1] that we have here to deal with a hematogenous icterus, is opposed first of all by the jaundice of the liver, which is invariably present, and not unfrequently intense, and, furthermore, by the oft-demonstrated presence of the biliary acids in the urine. But although the theory of icterus from resorption is at present almost universally accepted, still there is a variety of views as to the precise locality in the bile-ducts of the impediment, by means of which is produced the obstruction of the secretion that leads to the resorption.

By some, a catarrh of the portio intestinalis of the ductus choledochus is supposed to be the cause. The signs of such a catarrh have, it is true, in a number of cases been found; but even then the excretory bile-ducts themselves were pale and collapsed, or contained, at most, a little yellowish fluid. Notwithstanding the existence of a condition like that just mentioned, the theory of biliary obstruction arising from the impervious state of the orifice of the choledochus would, at all events, derive support from the hypothesis (of Pastau, suggested with reference to a similar condition of the bile-ducts in a case of

[1] Lehrb. d. pathol. Gewebelehre. 5. Aufl. S. 406.

phosphorus poisoning), that during the last stage of life the secretion may have been completely arrested, and that the bile previously accumulated may have been reabsorbed even up to the occurrence of death. It is, surely, very improbable, however, that life should be prolonged not only until the bile-secretion has been completely dried up, but until every trace of the secretion has been also reabsorbed from the bile-ducts; in chronic icterus, due to closure of the excretory ducts, when this process has progressed to extensive degeneration of the hepatic cells, the bile-ducts above the seat of the obstruction are found everywhere still filled with dark bile. That even in acute atrophy of the liver the formation of bile continues—naturally in constantly diminishing quantity—until the end of life, is indicated by the intensity of the icterus, which commonly increases until the last; by the occurrence of bilious vomiting; by the stools colored with bile even in the second stage of the disease; and by the detection, upon post-mortem examination, of bile in the small intestine, as described by many observers.

In the large majority of cases the absence of any swelling or of any mucous coagulum in the duodenal portion of the choledochus, the emptiness and paleness of all the bile-ducts visible to the naked eye, and the fact that the contents of the gall-bladder are composed but to a slight extent of bile, or consist purely of mucus, all tend to preclude the idea of an ordinary catarrhal icterus, and justify the supposition that the impediment to the elimination of the secretion may be located in the interlobular ducts, or still further above in the immediate vicinity of the source of the secretion. Buhl is of the opinion that the jaundice is to be referred to the obstruction of the finest bile-ducts by the fatty degeneration and desquamation of their epithelium observed by him (subsequently also by Bollinger and Perls), as well as by the compression of these ducts induced by the inflammatory swelling of the interstitial structure. Frerichs and Bamberger locate the impediment in the periphery of the hepatic lobules; the former affirms that the bile-ducts at their origin are compressed by the free exudation which he assumes to be present; the latter considers that these ducts are occluded by the detritus from the peripheral hepatic cells. It is obvious that all the above-

mentioned processes must result in a stagnation of the secretion in the hepatic lobules, or in those central portions which are still performing their functions; and it is quite possible that at certain times one, and at other times another of these processes, or even several simultaneously operative, may constitute the mechanical factor in the production of the icterus. The subsequent resorption of the bile-pigment contained in abundance in the detritus may also contribute toward intensifying the jaundice; that this process occurs is proved by the absence of the icterus in the red substance (*vide* p. 253).

The immediate cause of the *severe brain symptoms* is not yet determined. It cannot be referred to gross alterations in the brain, inasmuch as in the majority of cases such changes are by no means present. The idea would, therefore, be suggested that we have here to deal with a substance which acts upon the brain in a manner analogous to certain poisons. According to a very old theory, and one that until quite recently has been maintained by distinguished authors (by Leyden most determinedly), it is the constituents of the bile that have passed over into the blood, and of these especially the *biliary acids*, which exercise this influence. For confirmation of this hypothesis, in accordance with which the brain-symptoms are commonly designated as cholæmic, we can refer to the positive results obtained by many investigators[1] from experiments with injections of filtered bile or biliary salts into the blood. The animals manifested disturbances of respiration, and sank into a soporific or comatose condition, which was frequently the forerunner of convulsions. But, apart from the circumstance that these experiments are opposed by others in which the result, so far as concerns the functions of the central nervous system, was a negative one,[2] they are, moreover, scarcely sufficient of themselves to afford any explanation of the mode of origin of the brain-symptoms in acute atrophy of the liver. Between the latter symptoms and those produced by the experiment there exists, in the next place, no trifling difference, in so far that, in case of the animals experi-

[1] *Kuehne*, *v. Dusch*, *Roehrig*, *Huppert*, *Leyden*. Vide *Leyden*, l. c., S. 57 ff.

[2] *v. Dusch*, l. c., S. 41, sub. 6; *Frerichs*, Klinik, Bd. 1, S. 240 u. 404; *Traube*, Ges. Abhandl., Bd. 2, S. 823; *Mueller*, Arch. f. experim. Pathologie, Bd. 1, S. 226 ff.

mented upon, there has never been observed any condition to be compared with the maniacal paroxysms. Then, too, the severe nervous derangements following the injection of the biliary acids only supervened when relatively large amounts had been injected, or when the injection was made directly into the *carotis*. If, in consequence of the ligation of the ductus choledochus, the biliary acids penetrate into the blood,[1] then the animals, notwithstanding their intense jaundice, are at most languid and dejected, but manifest no indications, even where the artificially produced disease terminates fatally, of the severe cerebral symptoms which were excited by the acute atrophy of the liver, and partly also by overcharging the blood with injected biliary acids. In like manner, these symptoms are wanting when the orifice of the bile-duct is impervious, owing to some pathological process; or they may not supervene until, after prolonged stagnation of the secretion, the hepatic cells have, for the most part, undergone disintegration.

It is, moreover, *à priori* impossible that in a disease such as acute atrophy of the liver, in which the formation of biliary acids gradually more and more diminishes, the action of these substances upon the brain should begin to manifest itself just at the close of life; while their influence upon the other portions of the nervous system—for instance, upon the ganglia of the heart, renders itself perceptible immediately after the appearance of the cholæmia. It should be added, that the cerebral symptoms occasionally make their appearance sooner than the icterus, and, furthermore, may be present, in characteristic form, even when the latter is altogether absent. (Compare the Observation of Bamberger, previously referred to, p. 268.) Now, to however slight an extent the absence of the icterus tends to preclude, even in these cases, the possibility that the cholæmia may have already begun, by just as little does anything point to an especially abundant accumulation of the constituents of the bile in the blood. The diminution of the urinary secretion, by means of which, according to the theory of Leyden, such an

[1] Vide *Leyden*, l. c., S. 83–90. Compare, also, *Feltz* and *Ritter*, Jour. de l'Anat., etc., 1875, p. 405 sq.

accumulation is produced, occurs, as a rule, at, or after, the beginning of the severe nervous symptoms.

Supported by the fact that the kidneys, along with the liver, are also uniformly affected by the parenchymatous degeneration, and that, in most cases which have been examined with reference to this particular, the quantity of urea contained in the urine in the later stages of the disease has materially diminished, or even ultimately disappeared altogether, certain writers (Rokitansky; also Frerichs) have enunciated the hypothesis that the brain-symptoms may be chiefly, or at least in part, of a *uræmic* character. But they exhibit, even in their external features, but slight analogy with the symptoms observed in uræmia. Whereas the uræmic convulsion is characterized essentially by epileptiform spasms with subsequent coma, in the combination of symptoms here the subject of discussion, spasms either assume a more subordinate position, or are altogether absent. (Whether these spasms make their appearance or not, depends possibly, to a large extent, upon the individual predisposition of the patient; this view is at least favored by the unmistakable influence exercised by childhood.) Upon the other hand, maniacal paroxysms, or conditions of psychical excitation allied thereto, and differing therefrom in degree only, are of such frequent occurrence that, as a rule—to borrow the language of Traube—the cholæmic convulsions take on a psychiatric form. Moreover, the kidneys fail to present in most cases, either as respects their function or their anatomical condition, such derangements as are found in those affections in whose train uræmia is more or less constantly developed; and, as regards the diminution or disappearance of the urea in the urine, it is much more probable, as will be presently shown, that the formation of this substance, and not its elimination from the blood, is impeded.

A third theory refers the origin of the cerebral symptoms to the *acholia.* More than thirty years ago the "retention within the blood of substances intended for the formation of secretions" supervening upon the arrest of the hepatic functions, was termed by Virchow[1] the most probable cause of the brain-symptoms in

[1] Virchow's Arch. Bd. 8, S. 363.

icterus gravis; and subsequently the same view has been maintained by other writers (Frerichs, Bamberger, Liebermeister). Still, in the blood of patients no substance has hitherto been found to which such an effect could with probability be ascribed. Austin Flint [1] believed that he had discovered such a substance in cholestearine. According to his theory, cholestearine is chiefly a product of metamorphosis of tissue in the nervous system, and to the liver is assigned the duty of cleansing the blood from this excrementitial matter, and of converting it into bile. If the liver is prevented by morbid changes from performing this duty, then the cholestearine retained in the blood—the cholesteræmia—gives rise to that condition which is usually designated by the term cholæmic intoxication. The actual fact involved in this theory is confined to the circumstance that in diseases in which the hepatic function is abated, or completely suspended, a remarkable increase in the amount of cholestearine contained in the blood has been repeatedly observed. But that this can exercise a toxic effect upon the brain is by no means proven; upon the contrary, it has been shown by clinical observations, and particularly, moreover, by the results of experiments, to be extremely improbable.

According to the statement of Flint, the blood of healthy adults contains 0.445–0.751 pro mille of cholestearine, but, on the other hand, in a case of cirrhosis of the liver with severe symptoms, 0.922; and in another case of the same disease attended by a universal and deep-seated change of the hepatic cells even 1.850 pro mille. Pagès relates a case of icterus gravis from the clinique of Feltz, where the examination of the blood likewise disclosed the presence of 1.85 pro mille of cholestearine. Picot (Jour. de l'Anat. et de la Physiolog., VIII., 3) discovered in the blood of a woman who had died of acute atrophy of the liver 1.864 pro mille, and in the brain 15.20. As regards the attempts to prove experimentally the second portion of Flint's theory, Pagès was unable to detect the slightest cerebral symptoms in dogs into the blood of which he had injected within a period of sixteen days as much

[1] Experimental Reserches on a new Excretory Function of the Liver. Gaz. des Hôp. 1868. No. 52 et 58.—Recherches expériment. sur une nouvelle fonction du foie consistant dans la séparation de la cholésterin du sang et son élimination sous forme de stercorine. Paris, 1868.—See further: *Tincelin*, Des principes biliaires. Thèse de Strasb. 1869.—*Pagès*, De la cholésterin et de son accumulation dans l'économie. Thèse de Strasb. 1869.—*Koloman Mueller*, Archiv für experiment. Pathol. Bd. 1, S. 213.—*V. v. Krusenstern*, Virch. Arch. Bd. 65, S. 410.—*Feltz* et *Ritter*, Jour. de l'Anat. et de la Physiol. 1875, p. 147.

as 2.75 grms. of cholestearine dissolved in soap-water; Feltz, moreover, saw no instance of brain-disturbance in the cholesteræmia which he had artificially produced. So, likewise, Krusenstern, who injected daily into the veins of dogs 10 c.ctm. of a 3 per cent. solution of stearin-soap, containing ½ per cent. cholestearine, found the condition of the animals unchanged in the slightest particular. Upon the other hand, K. Mueller, in nine experiments upon dogs, observed invariably after the injection of 4.5 centigrms. of cholestearine dejection, difficulty of respiration, and of voluntary motion, reduction of peripheral sensibility and coma, and in one experiment there was even noticed a condition bearing the closest resemblance to a maniacal paroxysm; but the liquid employed by him for the purpose of injection was a thick-fluid mixture, composed of soap-water and extremely finely-divided, but *not dissolved*, cholestearine!

Frerichs alludes to the possibility, that among the products of the disintegrated glandular substance passing into the blood, there may be contained substances which are concerned in the production of the brain-symptoms. No such influence is exerted by leucin and tyrosin; these substances were injected into the blood of animals in great quantities, both by the above-mentioned experimentist, as well as by Panum[1] and by Billroth,[2] without giving rise to any disturbances of the nerve functions.

Traube has attempted an explanation of the severe cerebral symptoms, which differs essentially from the hypotheses thus far discussed. According to his view, the cholæmic convulsions have the same origin as those very transitory mental derangements, such as appear often in the form of mania, which are not unfrequently observed toward the close, or after the crisis, of an acute disease running a very rapid course, especially pneumonia; and, from the fact that they are due to an imperfect nutrition of the cerebral substance, they are termed the delirium of inanition. This theory is, in my opinion, one in favor of which much can be said. When once the same, or approximately the same, factors, which render acute inanition of the brain the probable cause of the complex symptoms in question, observed in the affections cited by Traube by way of comparison—when these factors are present in acute fatty degeneration and atrophy of the liver, and at times even in a higher degree than in the former diseases—then here, as well as there, are seen to appear in acute form de-

[1] Schmidt's Jahrbb. Bd. 101, S. 215. [2] Langenbeck's Archiv. Bd. 6, S. 396.

rangements of the digestive functions, insomnia, parenchymatous degeneration of numerous organs, weakness of the circulation, and diminution in the relative number of the red corpuscles; and as respects the influence of these pathological processes upon the nutrition and functions of the brain, it must be in itself unimportant whether they have been established as the after-effect of a severe fever, or in some other manner. Still, on the other hand, the difference in their mode of origin is very well adapted to explain the difference in the symptoms which mark their progress; in those severe febrile affections the violent cerebral manifestations subside, because the alterations which constitute their exciting cause become retrogressive after the cessation of the fever; in the disease with which we are here concerned, they are, almost without exception, the forerunner of death, from the fact that in the last instance they are dependent upon a process that is wont to advance continuously. The theory of Traube is recommended, moreover, by the circumstance that with its assistance we can comprehend why the clinical features of the brain-symptoms, which in most cases are so characteristic, are in many other instances less distinctly marked; and why their most significant characteristics—the loud delirium and the maniacal convulsions—are, at times, wanting, where the course of the disease is acute, as well as where it is more protracted. For, obviously, an imperfect nutrition of the brain is more likely to manifest gradual variations and even essential differences, accordingly as the advance of this process is more rapid or protracted, and according to the individuality of the person affected, than is the deadly action of a brain poison.

The diminution in the *quantity of urine* during the last days of life is to be attributed in part to the acute fatty degeneration of the epithelium of the kidneys, and in part to the circumstance, that, in consequence of the fatty degeneration of the muscles of the heart, the blood pressure in the aortic system is reduced. The most striking anomalies in the *chemical constitution of the urine* are connected with the processes of oxidation and metamorphosis of matter within the organism. While the quantity of urea sinks gradually to the minimum, there appear in the urine nitrogenous and non-nitrogenous substances, which are easily ox-

idizable. Several of these—lactic acid, creatin, the peptonoid substances, and the extractive matter soluble in alcohol—belong to the normal products of the intermediate metamorphosis of matter, the interrupted oxidation of which furnishes an adequate explanation of their passage into the urine. Tyrosin, on the other hand, from which it is conjectured that oxymandel acid is also formed, is not usually present within the system, and it may be considered an established fact, that this substance is produced by an abnormal metamorphosis of the organic albumen in the higher grades of parenchymatous degeneration. Leucin has in part, surely, the same origin, making its appearance regularly, as is well known, along with the tyrosin, upon the decomposition of animal substances containing a large proportion of nitrogen. But, upon the other hand, in so far as this substance forms a normal constituent of most glandular organs, and as such represents a product intended for the formation of the urea, we can hardly avoid tracing a connection between its appearance in the urine and the absence of the urea, and regarding a portion, at least, of the leucin as representative of the urea. That the actual production of the latter substance, and not merely its elimination from the blood, is interfered with, is extremely probable, because in other diseases, in which the degeneration and functional derangement of the kidneys is quite as considerable as it is here, such a disappearance of the urea from the urine is not observed.

Hemorrhages, as a rule, at several, not unfrequently at very numerous points, occur so frequently that a more or less pronounced *hemorrhagic diathesis* must be designated as a pretty constant feature of the disease. The cases in which the hemorrhages appear to be confined to the parts drained by the roots of the portal vein, form too small a minority to justify our ascribing to the obstruction presented to the circulation in the liver by the collapse of the parenchyma any other signification than that of a secondary factor, which tends to favor the production of the hemorrhages. But its influence renders it intelligible why hemorrhages occur with decidedly greater frequency in the organs from which the portal vein derives its blood, than in the others. And, analogously, an explanation is also afforded why the bleedings take place almost exclusively during the last days

of life ; for at this period the retardation of the circulation, resulting from the degeneration of the muscular tissue of the heart, necessarily gives rise to an over-distention of the veins and capillaries. To what the hemorrhagic diathesis is due, we are no better able to accurately determine here, than in case of most other diseases where it is found. Although one would not unnaturally suppose, that the same process, which gives rise in many other organs besides the liver to granular degeneration, may induce also analogous alterations in the walls of the blood-vessels, and reduce thereby their capacity of resistance to the blood-pressure, still, in the disease here under consideration nothing abnormal has as yet been demonstrated in the histological character of the smaller vessels. Upon the other hand, there can be no doubt that the blood deviates in many respects from the normal condition. This is evinced chiefly by its diminished coagulability, which was at first pointed out in most instances, it is true, in the cadaver, and might, therefore, be regarded[1] as a result of the loss of blood ; but it was also observed where no such loss had been sustained, and in the case of Horaczeck, above (p. 270) alluded to, it occurred several days previous to the appearance of any appreciable hemorrhage whatsoever. Furthermore, the blood contains substances, which under normal conditions are either altogether wanting, or at least are not present in such a quantity as must be the case in a disorder by which the function of the largest glandular organ is materially impaired. Among the substances of the former class there has been ascribed chiefly to the biliary acids an influence in the production of the hemorrhages ; and, indeed, this theory derives support from the occurrence, observed by Leyden and others, of recent hemorrhages in numerous organs (brain, conjunctiva, aqueous humor, pulmonary pleura, intestines, kidneys) after the injection of biliary acids into the blood. When it is considered, however, that it is precisely those cases running a more protracted course in which, notwithstanding the prolonged existence

[1] The proportionate increase in the number of white corpuscles observed by some authors is, in all probability, to be referred to the diminution of the red discs produced by the hemorrhages.

of a severe icterus, the hemorrhages are frequently absent, whereas, when the course is peracute and the icterus but slightly developed, they are occasionally so extensive, one would hardly be inclined to regard the action of the biliary acids that have passed into the blood as the sole cause of the hemorrhagic diathesis. The other substances abnormally contained in the blood, we are either not at all acquainted with, or, at least, are not familiar with their influence upon the walls of the vessels. As it has been demonstrated, however, by Cohnheim, that even a comparatively brief interruption of the supply of fresh blood to those vessels which are supplied with no *vasa vasorum* of their own, occasions an abnormal permeability to the red corpuscles, it may, indeed, be assumed as highly probable, that contact with blood that has been considerably altered in its composition may have the same effect.

The *swelling of the spleen* has been traced in part to the abnormal composition of the blood, and in part to the derangement of the hepatic circulation. The anæmic and collapsed condition displayed by the hepatic parenchyma upon post-mortem examination, leaves no doubt as to the existence, during the last days of life, of a considerable impediment to the outflow of blood from the portal vein. But the circumstance that the splenic enlargement already exists before the collapse of the liver, and more particularly the anatomical character of the tumor and its coexistence with a parenchymatous degeneration affecting numerous organs, renders it probable that its origin is to be referred chiefly to a qualitative alteration of the blood, and that the obstruction in the portal vein is to be considered, at the most, as a subordinate factor.

Theory as to the Disease.

As respects the nature of the *anatomical process in the liver* which leads to the wasting of the gland, two opposite theories confront each other. According to one theory, which was first enunciated by R. Bright, and subsequently subscribed to by Wedl, Buhl, Bamberger, Frerichs, Oppolzer, Lebert, Foerster, Liebermeister, Riess, and others, this process is an acute diffuse

inflammation. It was conjectured even by Bright that the secreting tissue may be thereby more implicated than the connective tissue, and by the majority also of other authors of repute the disease is regarded as parenchymatous hepatitis in the sense employed by Virchow.

In opposition to the above view, Rokitansky, Henoch, v. Dusch, Leyden, Zenker, Klebs, Ackermann, and others, considered the process not an inflammatory one, but saw therein merely a retrogressive metamorphosis of the glandular elements.

If we direct our attention merely to the granular degeneration, the latter theory accords, indeed, with the present status of our ideas respecting inflammation, in so far as the swelling of the gland-cells conjoined with the granulation of the protoplasm can no longer be accepted as evidence of an exudation that has taken place into their substance. Still, manifold changes have been detected besides the granular degeneration which seem to point to an inflammatory origin of the affection. Least of all is this true, however, as regards the free exudation which Frerichs believed he had detected in the form of gray rims at the periphery of the lobules, at points where the process had not yet advanced to atrophy. The circumstance that the finely granular material of which these rims consisted, enclosed isolated hepatic cells in a state of disintegration, leaves hardly any doubt that they themselves are none else than the detritus of cells already disintegrated. Of greater significance is the recent diffuse hyperplasia of the interstitial connective tissue, and its infiltration with lymphoid cells. The former, it is true, is not of infrequent occurrence, but, still, is by no means uniformly present; moreover, in cases where it is confined to the red substance (*vide* p. 254) it can, obviously, only be regarded as a secondary process. Fine-cellular infiltration has hitherto been seen[1] only in a few primary cases, and the observation of Lewitski and Brodowski, according to which, along with the fine-cellular infiltration, a proliferation of the hepatic cells and subsequently of the intralobular blood-capillaries takes place, stands completely iso-

[1] In secondary cases—in puerperal fever—this was observed by *Buhl* as early as 1856, and has been recently seen by *Dupré*.

lated. For the present, therefore, we must restrict ourselves to the statement, that there are cases in which the theory, that the acute atrophy of the liver originates in an inflammation (in the narrow signification of the word), appears admissible, but that those cases constitute the majority—even when we consider merely those instances in which an accurate histological examination has been made—in which no alterations of a decidedly inflammatory character have been demonstrated. Those rarer examples belong exclusively, at least with the exception of an observation of Winiwarter (*vide* p. 259), to the variety termed red atrophy.

As respects the *pathogenesis* of acute atrophy of the liver, numerous theories have been enunciated; many of which have at present only an historical interest. As, for example, the notion that the disease originates in the passage of the biliary elements into the blood of the portal vein (Rokitansky); in a polycholia (Henoch); in a closure of the portal vein (Henle); or in a paralysis of the bile-ducts (v. Dusch); so, likewise, the theory foreshadowed by Budd, and more elaborately developed by Lebert, that in consequence of a blood-poisoning[1] the liver experiences first a considerable impairment of its function, as a result of which, as happens in case of other organs whose functions are imperfectly performed, it begins to be atrophied. A more intimate investigation of these hypotheses is the less necessary, inasmuch as they have long since been recognized as untenable, and have in part been subsequently abandoned even by their authors. None the less inadmissible is the hypothesis brought forward by Rokitansky (in the third edition of his Handbook), that the affection is based upon a deranged innervation of the liver, in consequence of which the secretory elements become broken up in their anomalous secretion. Klebs[2] divided the hepatic nerves without finding disintegration of the hepatic cells thereby produced.

In accordance with the view now most generally adopted, a constitutional disease forms the starting-point of the acute atrophy of the liver. Thus, the production of disturbances in the

[1] *Lebert* compared this poisoning to that which gives rise to the typhoid processes, and would, therefore, term the severe form of icterus *icterus typhoides*.

[2] Tagebl. d. 45. Vers. Deutscher Naturforscher in Leipzig. 1872. S. 223.

liver is regarded by Buhl as one of the evidences of an impaired nutrition of the entire organism, which attacks particularly the heart and kidneys. According to Wunderlich, it is an acute pernicious (malignant) constitutional affection by which the process of destruction is excited in the liver, and generally at the same time also in other organs. Bamberger, too, who formerly regarded the disease as primary hepatitis, has at a subsequent period admitted that it may be included in the category of severe constitutional diseases, and that the anatomical alterations in the liver may be considered as secondary and induced processes.

This idea is favored, above all, by the circumstance that, along with the liver, the kidneys and the heart, and, as is extremely probable in view of more recent observations—as yet isolated, it is true—numerous other organs (*vide* p. 260) are also invariably found in a condition of granular degeneration. The presence of similar changes at such different points of the body tends to force us, indeed, to the conclusion, that the separate local affections are to be considered as concomitant effects of the same cause. It may be, furthermore, stated in confirmation of the theory in question, that in many acute, general, infectious diseases (pyæmia, typhoid fever, recurrent fever, bilious typhoid fever, yellow fever) the granular degeneration of the liver now and then attains so high a grade, that the condition of the organ approximates closely, or completely resembles, that presented in idiopathic acute atrophy of the liver. It must, indeed, be admitted that, in view of the insignificant amount of fever present, idiopathic acute atrophy of the liver could hardly be classified among the acute general infectious diseases, in the restricted sense. Upon the other hand, it presents, not only as regards the behavior of the bodily temperature, but also in many other respects, a striking analogy with acute phosphorus-poisoning; and we are therefore justified in the assumption, that it has its origin in the action of a poison, which, in a similar manner to phosphorus, by interrupting the oxidation and interfering with the metamorphosis of albumen, produces the parenchymatous degenerations and the abnormal products of the metamorphosis of tissue.

Some authors (Davidson, Gerhardt) are disposed to attribute the acute atrophy of the liver, at least in a portion of the cases,

to poisoning by biliary acids. It is maintained by them that there exists, at the outset, a catarrhal jaundice, and that thereby the reabsorbed biliary acids, being insufficiently eliminated through the kidneys, accumulate to such an extent in the blood as to induce the fatty degeneration of the liver and other organs, as well as the brain-symptoms and the hemorrhagic diathesis. But even Leyden, who, indeed, likewise referred the alterations of the heart and kidneys and the severe symptoms of the disease to the accumulation of bile in the blood, regards it, nevertheless, as inadmissible that the anatomical process in the liver should be referred to the same cause; since, in the experiments upon animals, connected respectively with the injection of biliary acids and the ligature of the ductus choledochus, fatty degeneration of the liver is, indeed, observed; but, on the other hand, in no instance is disintegration of its cells detected, and still less any condition corresponding to that of acute atrophy of the liver. However much, in most cases, the clinical characteristics in the prodromal stage may seem to favor the idea that the affection originates in a simple catarrhal icterus, still, as has been shown above (p. 281), weighty considerations stand opposed to this theory. If one is inclined, nevertheless, to adhere to this view, it will then be necessary to assume, as has been done by Zenker, the supervention of still other, and as yet unknown causes, by whose agency the malignant transformation of the originally benign icterus is brought about. For if the destruction of the red corpuscles by the biliary acids were so extensive as to justify our attributing to the oligocythæmia thereby induced the nutritive disturbances in the liver, then, in all probability, we should find, too, an accumulation of hæmoglobin crystals in the urinary canals. Now, such an accumulation has, indeed, been observed by Hoppe[1] in a dog, into whose jugular vein a large quantity of choleate of soda had been injected, but never, on the other hand, in a case of acute atrophy of the liver.

In opposition to this notion, that the acute atrophy of the liver is the concomitant of a constitutional disease, it may be urged that the granular degeneration, while implicating, indeed, numer-

[1] Virchow's Archiv. Bd. 25, S. 183.

ous organs, is, nevertheless, invariably much further advanced in the liver than in any other organ, and that the development of the characteristic symptoms appears to be associated with the higher grade of hepatic changes. Upon these data is based the theory of those who, like Frerichs, Sander, Demme, Liebermeister, Rosenstein and others, transfer the real seat and starting-point of the disease to the liver; and if they, too, assume the action of a poison to be the cause, they, nevertheless, regard this organ as the one primarily diseased, and the anomalies of the metamorphosis of tissue as but secondary processes induced by the functional derangement of the liver. This view would be rendered much more probable, if future observations should reveal the existence in the liver of a similar condition to that recently reported by Winiwarter and Lewitski, and Brodowski, or if the opinion of Klebs were confirmed, according to which the disease is induced by the invasion of bacteria proceeding from the gall-ducts.

The varieties of the anatomical picture (simple disintegration, fatty disintegration; yellow atrophy, red atrophy) and the duration of the disease, fluctuating within very distant margins, lead to the conclusion, that there are various noxious influences which may be the cause of the affection. The fluctuations in question might perhaps with equal propriety, however, be ascribed to the variations in the extent of these noxious influences. But then, too, the degree of the individual capability of resistance will prove not without influence upon the occurrence and more or less rapid development of the disturbances. Thus, the relatively great frequency and the almost invariably rapid course of the disease in pregnant women is probably due to the circumstance that, even pregnancy, of itself, involves a greater predisposition to parenchymatous degeneration of the glandular organs, especially the liver and kidneys. A similar predisposition, resulting from pre-existing faulty nutrition of the hepatic cells, is suggested, moreover, in those cases where the acute atrophy of the liver supervenes during some chronic hepatic disease (cirrhosis, cyanotic induration, etc.).

The conception of an idiopathic acute atrophy of the liver involves, strictly speaking, the presumption, that there is a dis-

ease in which the granular degeneration of the liver gives rise to wasting of the gland, not merely in isolated cases—as in the above-mentioned acute infectious diseases—but uniformly, that is, as a necessary result of the nature of the specific cause. But is this wasting to be really accepted as something pathognomonic? There occur cases of general acute fatty degeneration, which accord with the majority of cases of idiopathic acute atrophy of the liver as respects the etiological relations (female sex, youthful age, unknown noxious influence), and also as respects the symptoms, even to the gradual variations; in these instances, however, the liver presents upon autopsy not wasting and collapse, but increased weight and acute enlargement. Such cases have been described by Rokitansky [1] as fatal steatosis of the liver and kidneys; by Wunderlich [2] as spontaneous, rapid, fatal, general fatty degeneration; by which terms must manifestly be designated something different from acute atrophy of the liver. Liebermeister, on the other hand, deems it the same disease which, at other times, does not terminate until the gland has wasted, and explains the anomalous character of the liver by assuming that here, in consequence of the brief duration of the disease, the parenchymatous degeneration has not reached its last stage. It is true, the fatal termination in the questionable cases resulted as early as from the fifth to the eighth day, but among the cases of idiopathic acute atrophy of the liver there are also observed not a few in which death supervenes quite as early, and even earlier. Moreover, those cases resemble so perfectly, clinically and anatomically, the ordinary cases of acute phosphorus-poisoning that by some writers the opinion (certainly unwarrantable) has been expressed that they, too, are likewise induced by the action of phosphorus. If, now, in Wunderlich's spontaneous, quickly fatal fatty degeneration the pathological process, as a whole, is the same as in idiopathic acute atrophy of the liver, then we cannot but admit the existence of a similar process also in acute phosphorus-poisoning. In opposition to this theory, the chief argument has been, that in

[1] Zeitschr. d. Ges. d. Aerzte in Wien. 1859. Nr. 32.

[2] Arch. d. Heilk. 4. Jahrg. S. 145.

acute phosphorus-poisoning the histological appearances observed in the liver correspond much more closely to the familiar picture of fatty infiltration, than to granular degeneration (Schultzen and Riess). But in phosphorus-poisoning, too, the cells in the beginning of their change present precisely the appearance that is commonly considered characteristic of granular degeneration. Besides, it would be generally impossible to draw a sharp line of division, according to the simple histological characteristics, between fatty infiltration and fatty degeneration. And if in the fatty-developed phosphorus liver, according to a statement of Perls,[1] the amount of fat has increased chiefly at the expense of the water, still the solid substance free from fat has also suffered a reduction, which is not less than in the case of acute atrophy of the liver[2] examined by the same investigator. It is probable that the hepatic cells, while they themselves under the action of the phosphorus are undergoing fatty degeneration, absorb more fat which proceeds from the other organs simultaneously attacked by fatty degeneration. When this does not take place in acute atrophy of the liver, it may be due to the circumstance, that here the parenchymatous degeneration makes its appearance in the other organs later than in the liver. (The large oil-drops appearing in the detritus, also in acute atrophy of the liver, may have been first formed by the coalescence of smaller drops rendered free by the destruction of the cells.) In other respects, the change in the liver in acute phosphorus-poisoning is demonstrated to consist chiefly of a degenerative process by the circumstance that in isolated cases, in which the duration of the illness is unusually long, extensive disintegration of the hepatic cells ensues, and, at points, complete resorption of the detritus.

But, although the nutritive derangement of the liver in acute phosphorus-poisoning is not essentially different from that observed in the idiopathic acute atrophy of the liver, yet it does not follow therefrom that the pathological process is also, as a whole, identical in both affections. The fact that a very decided majority of the cases of acute phosphorus-poisoning terminate

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[1] Lehrb. d. allgem. Pathol. 1. Th. Stuttg., 1877. S. 173. Nr. 15.

[2] Ibidem, S. 172. Nr. 12.

fatally, while the liver is still enlarged, appears to indicate that the changes in the other organs are here more extensively implicated in the production of the fatal event, than is the case in idiopathic acute atrophy of the liver. That the process which constitutes the fundamental cause of the latter affection may lead to death in quite as early a stage of the hepatic changes as commonly happens in phosphorus-poisoning, is an hypothesis which, to say the least, has not yet been proved. If one should be inclined to regard the cases of Wunderlich's spontaneous, rapidly fatal fatty degeneration as affording proof of this theory, it may be urged, on the other hand, that these cases form quite as rare exceptions as do those instances in acute phosphorus-poisoning in which an extensive atrophy of the liver is developed.

But although one were to include under the head of acute atrophy of the liver, as has been done by me in this treatise, only those cases in which the greater part of the secreting cells are destroyed as a result of a high grade of granular degeneration, and in which, in consequence of the resorption of their detritus, the organ experiences a perceptible reduction in consistence and volume—it remains, nevertheless, very questionable whether, in reality, where this process originates from unknown causes, one and the same disease is uniformly present. The circumstance, that in a portion of the cases the granular degeneration appears to be the result of a diffuse hepatitis, whereas in the others we have to deal from the outset with a retrogressive metamorphosis, would even now indicate, that "idiopathic acute atrophy of the liver" is a collective name for different morbid processes.

Diagnosis.

In its first stage, the recognition of the disease is, in the present state of our experience, impossible. Although certain symptoms, such as vomiting, great prostration, agrypnia, make their appearance more frequently here than in simple catarrhal jaundice, yet in the latter affection they are by no means such rare developments as to allow our inferring therefrom even the probable existence of the severe disorder. Such a supposition is

rendered much more justifiable by the appearance of jaundice during pregnancy.

The first decided indication is usually obtained by the circumstance, that icterus is superadded to the cerebral symptoms or hemorrhages. Still, it must not be forgotten that hemorrhages from the nose and gums, as well as vertigo, restlessness, and even delirium, occasionally appear even in those cases of jaundice which, in view of their otherwise mild course, we are not justified in classifying with the disease here under discussion.

In the second stage, the features of the disease generally become very soon so characteristic that the diagnosis presents no difficulties. The icterus, the hemorrhagic diathesis, the brain-symptoms, the absence of fever, the rapid diminution in the hepatic dulness, the splenic tumor, and the peculiar changes in the urine, constitute a train of symptoms which is not precisely repeated in any other disease. But these symptoms, it is true, are not all present in each individual case. Where the reduction in the volume of the liver—either because it is too slight, or owing to the existence of meteorismus—cannot be determined, and the urine contains neither leucin nor tyrosin, the diagnosis remains uncertain; though in this respect the absence of one or the other of the remaining symptoms is not important. The latter occasionally make their appearance also in many other diseases in which granular degeneration of the liver assumes merely a subordinate position in the pathological process, taken as a whole: for example, enlargement of the spleen, icterus, brain-symptoms and hemorrhage in typhus fever, puerperal fever, endocarditis ulcerosa; icterus and brain-symptoms in pyæmia, pneumonia, peritonitis. It will, however, prove easy to avoid confounding these diseases with acute atrophy of the liver; for, apart from the other distinguishing characteristics, which upon careful examination should never altogether escape notice, the state of the bodily temperature affords a certain clue to the differential diagnosis. All the last-mentioned affections are associated with fever, which is in the majority of them considerable, and runs a characteristic course; whereas in acute atrophy of the liver, during the second stage, there is throughout, or at least at the outset, complete absence of fever.

If our attention is directed solely to clinical observation, acute atrophy of the liver cannot always be distinguished from acute phosphorus-poisoning. Indeed, the remission of the pathological symptoms, preceding by several days the appearance of the severe developments—which remission is, in acute phosphorus-poisoning, almost uniformly observed—is commonly altogether absent in acute atrophy of the liver, or at least is but faintly marked; and, on the other hand, the grave symptoms in phosphorus-poisoning begin, as a rule, simultaneously with the icterus, whereas the latter, in the majority of cases of acute atrophy of the liver, exists even days or weeks previous to the appearance of the second stage. These differences in the course of the disease are, however, not decisive, and frequently cannot be turned to account as respects the diagnosis, from the circumstance that the patients come first under medical observation at so late a period, that their psychical condition does not permit their previous history to be accurately elicited. In the last stage of both diseases the appearances may be perfectly similar; and not only in those which relate to the icterus, the hemorrhagic diathesis, and the brain-symptoms, but also in all other respects. For in acute phosphorus-poisoning, also, this stage is generally free from fever, and is wont to present, toward the end of life, either a subnormal or a rapidly increasing temperature. In this affection, too, there has been demonstrated in the urine the presence of peptonoid bodies, abnormally abundant extractive matter, and sarco-lactic acid, associated with a considerable diminution in the amount of the urea (Schultzen and Riess), and in several instances even tyrosin and leucin (Wyss,[1] Ossikovsky[2]), and finally there appears here, likewise, a diminution in the volume of the liver, appreciable even during life.[3] This latter occurs, however, in phosphorus-poisoning only in quite exceptional instances, and never makes its appearance so early in the course of the disease, as frequently happens in acute atrophy, in consequence of which, when this reduction can be distinguished before the expiration of the first week, phosphorus

[1] Schweiz. Zeitschr. Bd. 3, S. 321.

[2] Wiener med. Presse. 1870. Nr. 50, 51.

[3] *Bollinger*, l. c., S. 152. *Schultzen* u. *Riess*, l. c., S. 7. Fall 1.

may with certainty be eliminated from the possible causes of the disease. The case is analogous with respect to leucin and tyrosin; the presence of any very large quantity of these substances in the urine speaks with great probability in favor of acute atrophy, and against phosphorus-poisoning.[1]

Duration, Termination, Prognosis.

Of 102 cases, in which the date of the commencement of the symptoms introducing the disease is accurately given, there terminated fatally:

Within 4 days	5,	all in pregnant women.							
Between the 5th and 7th days	18,	of these	10	"	"				
Between the 8th and 10th days	14,	"	4	"	"				
Between the 11th and 14th days	17,	"	6	"	"	and	1[2]	with red atrophy.	
Between the 15th and 19th days	9,	"	2	"	"	"	2[3]	"	"
At the expiration of the 3d week	13,	"					5	"	"
In the 4th week	6,	"					2	"	"
After 4–4½ weeks	10,	"					7	"	"
" 5–8 "	10,	"					6	"	"

It will be seen from the above table that the duration of the disease generally fluctuates within very wide limits, but that nearly one-half of all cases terminate within from the third to the fifth week; in but ten per cent. only is the disease protracted into the second month. A duration of a few days occurs only in pregnant females, for usually with them the course of

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[1] In a case of acute phosphorus-poisoning published by *Fraenkel* (Berl. klin. Wochenschr., 1878, Nr. 19), just as this work is passing through the press, occurring in *Leyden's* clinique, in which death resulted at the expiration of the second week's illness, and the liver, whose reduction in bulk could be demonstrated as early as the third day previous to the last, presented in both lobes points of red atrophy, leucin and tyrosin were found in abundant quantity in the urine.

[2] *Rehn*, 2¼ years. Boy. Death on thirteenth day.

[3] *Fick*, two observations. *Lewitski* u. *Brodowski*.

the disease is invariably an acute one in the narrower signification of the term, and in extremely rare cases does it extend beyond the second week. Extensive red atrophy appears to occur, in extremely rare instances, where the duration is less than three weeks; upon the other hand, a decided majority (of twenty, at least thirteen) of the cases having a duration of four weeks and more is composed of those in which the process has attained this extreme degree.

The period between the appearance of the grave symptoms and death, amounts most frequently to from one and one-half to three, far less often to from four to seven days, and only in quite exceptional cases to more than one week.

Among the 118 observations which afford us information on this point, for the second stage a duration of 24 hours or less is found in 10; of 1¼–2 days in 46; of 2½–3 days in 26; of 3½–4 days in 17; of 5–7 days in 15; of 9 days in 2; and of 10 and 14 days in 1 each.

Where the second stage continues less than twenty-four hours, it may commonly be assumed that death will approach more rapidly on account of the weakening hemorrhages from the uterus or stomach. Where, on the other hand, this disease is protracted to an unusual length, the cerebral symptoms are, as a rule, at the outset less severe, or else they exhibit well-marked remissions.

According to the difference in the duration of the disease, the cases may be divided into peracute, moderately acute, and protracted. The division of the disease into an acute and a chronic form, as has been favored by Eppinger, seems to me inadmissible; for so numerous intermediate grades are found between the shortest and longest duration, that it would prove very difficult to draw the dividing-line.

Whether the disease can terminate otherwise than fatally, is questionable. There is contained in the literature a number of observations relatively not altogether small, which have been recorded as proofs of the occurrence of a favorable termination. Now, although these examples may give rise to well-founded doubts respecting especially the diagnosis, yet there are some among them in which no other objection can be urged with re-

gard to the diagnosis, than the mere fact that they have terminated in recovery. Such cases have been communicated by Frerichs,[1] Schnitzler (from Oppolzer's clinique[2]), Leichtenstern,[3] Jones.[4]

In these cases, the signs of diminution in the volume of the liver, as well as the characteristic derangements of the brain functions, and generally also hemorrhages had already supervened before the change for the better had set in; in Schnitzler's case, the presence of leucin and tyrosin in the urine had even been detected.[5] The convalescence progressed at a comparatively rapid rate (within one to two weeks). In the two cases most accurately reported, those of Schnitzler and Leichtenstern, the liver was atrophied even at the date of the patient's discharge.

À priori the possibility of the termination in recovery cannot be questioned. If the process does not run an altogether too acute course, we can, indeed, imagine that there is a point of time, when the destruction of the hepatic parenchyma has already progressed far enough to cause an appreciable reduction in the volume of the organ, and a condition of the blood tending to affect the nutrition of the central nervous organs, the permeability of the walls of the vessels and the composition of the urine, and that yet, on the other hand, sections of the gland capable of performing their functions are still present to such an extent as to suffice for the prolongation of life. Should the process now be arrested, then the degeneration at those points where it has begun to attain a slight grade may become retrogressive, and the cells that have undergone complete destruction may be replaced by new-growth. Whether the peculiar rows of cells frequently observed in the most atrophied parts of the organ (*vide* p. 254) can be considered the commencement of such a process, is, it must be admitted, not yet fully determined; but that a regeneration of the hepatic parenchyma under similar circumstances really does take place, is shown by the appearances obtained by

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[1] Klinik. Bd. 1, S. 231. Bd. 2, S. 18.

[2] Deutsche Klinik. 1859. S. 285.

[3] Zeitschr. f. ration. Med. Bd. 36, S. 241.

[4] British Medical Journal. May, 1872.

[5] Leucin was found in the urine by *Radziejewski* also (Virch. Arch., Bd. 36, S. 13), in a case of icterus gravis, which terminated in recovery.

C. E. E. Hoffman[1] in the liver of individuals who had died during the period of convalescence from severe typhoid fever; this writer counted here a far greater number of cells containing two and three nuclei, than is seen in the normal liver, and not a few, also, with four and five nuclei; and he observed in addition a very large number of remarkably small cells containing a single nucleus. Nevertheless, we must agree with Bamberger in considering the anatomical evidence of the healing process in acute atrophy of the liver as not yet forthcoming, and the occurrence of a favorable termination of the same as not proven.

But even if one is inclined to accept the above-cited cases as examples of recovery, they constitute, nevertheless, extremely rare exceptions to the rule, forming not two per cent. of the total number, and the prognosis of the disease is, notwithstanding, almost absolutely fatal.

Treatment.

In the first stage it is obvious that the same treatment is indicated as in acute gastric catarrh and catarrhal icterus. As soon as the more serious symptoms manifest themselves, the dangerous condition demands a more vigorous procedure. Starting upon the presumption that we are here confronted with an inflammatory process in the liver, attempts have been made, by means of drastic cathartics, and occasionally also by means of emetics (Corrigan), as well as by local and general abstractions of blood, to reduce the supposed congestion of the gland. Even after the development of the second stage, strong purgatives were administered, and, with the view of combating the hemorrhagic diathesis, the mineral acids. Moreover, for the purpose of allaying the separate severe symptoms, the remedies corresponding to the *indicatio symptomatica* were employed: to check the vomiting and hiccough, small pieces of ice, drinks containing carbonic acid, subnitrate of bismuth, blisters to the gastric region; to relieve the symptoms of cerebral irritation, cold applications and leeches to the head, stimulating enemata, morphine; to remove the symptoms of depression of the nervous system, cold douches

[1] Unters. üb. d. Veränd. d. Org. beim Abdominaltyphus. S. 216 ff.

and epispastics; for hemorrhages from accessible organs, cold applications, astringents, plugging; to prevent collapse, analeptics.

It must be admitted, however, that no substantial result has ever been attained by this mode of treatment. For, among the total list of cases in which it has been resorted to, the number of recoveries is so insignificantly small, that even if the correctness of the diagnosis is not called in question, yet any influence upon the favorable result appears extremely doubtful. In the case related by Leichtenstern (*vide* p. 303), from the clinique of Oppolzer, which is the most likely to pass for a case of recovery, the medication consisted simply in the administration of a mild purgative of calomel and jalap. The remaining cases above referred to, which resulted in recovery, agree with one another as respects their treatment, in so far that in all of them drastic cathartics were repeatedly resorted to; laxative remedies would, therefore, still be the most advisable. Abstractions of blood are manifestly opposed by the *indicatio morbi*, for by the diminution of the red corpuscles the parenchymatous degeneration can only be promoted; as a symptomatic remedy they afforded, at most, very transitory relief, but usually no appreciable benefit whatsoever.

As regards a case of Teissier, in which (according to Ozanam) aconite, and that of Lebert, in which benzoic acid with musk in large doses, is said to have effected a cure, no detailed accounts are submitted; in consequence of which we are not enabled to form an opinion either as to the correctness of the diagnosis, or the probability of the alleged influence of the medication.

Simple Atrophy of the Liver.

Rokitansky, Handbuch d. pathol. Anat. Bd. 3, S. 314. Lehrb. d. pathol. Anat. Bd. 3, S. 244.—*Virchow*, Arch. für pathol. Anat. Bd. 5, S. 290.—*Cohn*, Guensburg's Zeitschr. V. 6. 1854.—*Ruehle*, Wien. medic. Wochenschr. 1855. S. 67.—*Frerichs*, Klinik. Bd. 1, S. 260–284.—*Bertog*, Greifswalder Beiträge. Bd. 1, S. 81.—*Murchison*, Transact. of the Pathol. Soc. XVIII., p. 152.—*Cohnheim* u. *Litten*, Virchow's Arch. Bd. 67, S. 153.

Etiology.—Total simple atrophy of the liver occurs as concomitant symptom of senile *marasmus* and similar derangements

of the general nutrition, such as are induced particularly by chronic diseases of the digestive organs in which the supply or resorption of the nutritive substances is decidedly and permanently diminished.[1] Why the liver does not invariably participate perceptibly in a general wasting of this character, is no more susceptible of explanation than the dissimilarity manifested by separate individuals as regards the senile involution of the various organs.

Frerichs has attempted to trace simple atrophy of the liver to some permanent impairment of the circulation in the capillary system of the gland; and he therefore affirms that the usual cause of the affection is a destruction of the capillaries of the acini. This is occasionally brought about, according to the observations of the above-named author, as a consecutive change in severe malarial fever, by the capillary vessels becoming plugged with flakes and granules of melanotic pigment, which have either floated from the spleen into the portal vein, or have been spontaneously formed in the blood of the latter. Frerichs is, furthermore, of the opinion that even hyperplasia or carcinomatous infiltration of Glisson's capsule, proceeding from carcinoma of the stomach and making its way along with the portal vein and its ramifications deep into the liver, may occasion obliteration of the portal capillaries; the manner in which this is accomplished is not evident, however, from the case reported in support of this hypothesis (l. c., S. 263, Nr. 23); and the condition of the capillaries observed therein, which were compactly crowded together and contained pigment-granules, may be quite as well considered the result as the cause of the destruction of the cells. Very questionable appears also the hypothesis, in accordance with which Frerichs attempts to refer the origin of the hepatic atrophy in chronic exudation-processes and ulcerations of the small and large intestine to an obliteration of the hepatic capillaries;

[1] I have ransacked the literature in vain for proofs of the statement of *Klebs* (Handb. d. pathol. Anat., S. 414), that simple atrophy of the liver appears in chronic poisoning by lead and quicksilver; as respects arsenic and antimony, however, *Saikowsky* (Virchow's Arch., Bd. 34, S. 80) has undoubtedly demonstrated, by experiments on rabbits, that in long-continued poisoning a reduction in the volume of the liver supervenes, resulting from atrophy of the cells.

this, he maintains, is effected through the agency of the portal vein, "which, according to the nature and manner in which its roots participate in the exudation-processes in the tissue of the intestinal mucous membrane, gives rise in one case to the so-called metastatic abscesses, and in the other produces occlusion of the capillaries and consequent atrophy of the liver" (l. c., S. 275).

In the opinion of Frerichs, chronic thrombosis of the portal vein may also entail results similar to those induced by the destruction of the hepatic capillaries.[1] I have found, however, in the literature no case which furnished proof that this lesion can lead to a diminution in volume, attributable to simple atrophy.[2] Indeed, observations are reported by Frerichs himself (l. c., S. 280, Nr. 30), by Cohn[3] and by Leyden,[4] where, notwithstanding that the obstruction of the portal vein was of long continuance, and had even extended far into the substance of the liver, the volume of the gland presented no diminution, and its cells were only "pale and with few granular contents," or "atrophied in the central portion of the acini," or "at all parts well preserved and distinct in their walls and contents, only in general smaller." It will be readily understood, that in occlusion of the portal vein there results far less functional derangement of the liver, than when the capillary net-work of the acini themselves is impervious; for the nutrition of the latter is effected not only by means of the portal vein, but also by the veins designated by Sappey its regular accessory roots, and to a very considerable extent by the hepatic artery; this, in the case described by Cohn, was dilated threefold.

In a manner analogous to that suggested by Frerichs, Bertog explains the mode of origin of atrophy of the liver in two cases, published by him, occurring in Ruehle's clinique in Greifswald.

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[1] Even *Cohn* (Klinik der embol. Gefässkrankh., S. 503) admits that when the occlusion of the portal vein assumes a chronic form the liver may become smaller.

[2] As regards the case related by *Botkin* (Virchow's Arch., Bd. 30, S. 449), where, according to the view of this author, in consequence of thrombosis of the portal vein first simple atrophy had been induced, and subsequently, with the co-operation of the latter, secondary cirrhosis, compare p. 172.

[3] Klinik der embol. Gefässkrankh. S. 497.

[4] Berl. klin. Wochenschr.. 1866. Nr. 13. 2. Beob.

These related to men, aged fifty-seven and forty-seven years respectively, in whom, as a result of chronic peritonitis, there existed dense cicatricial tissue at many points of the mesenterium and the rest of the peritoneum, by which growth numerous radicles of the portal vein were compressed. The opinion expressed by Bertog, that the diminished supply of blood to the portal vein may here have been the cause of the derangement of nutrition and of the ultimate wasting of the liver, is hardly tenable, in view of the fact, that even in complete occlusion of the portal vein the nutrition of the gland is not materially impaired. It appears much more probable that here, also, the atrophy of the liver is to be attributed to the general marasmus which was present in a high degree in both patients, and which is adequately explained in one case by the existence of exhausting diarrhœa, and in the other by a stenosis of the pylorus. Indeed, even in two cases reported by Frerichs, there were similar, although less extensive, alterations of the peritoneum,[1] but there existed, besides, cachexia and general dropsy, which had been developed consecutive upon an ulcerative condition of the intestines.

Pathological Anatomy.—Simple atrophy of the liver entails a uniform reduction in the volume of the organ in all dimensions, as a result of which it undergoes no essential alteration in its form. It may be diminished thereby to one-half its normal volume. If the reduction in size is one of high degree, then the anterior margins often appear more decidedly reduced in thickness than the other portions of the liver, and frequently form a ribbon-like, thin rim, which is then composed exclusively of connective tissue.

The resistance is usually somewhat increased, which is particularly noticeable upon section, and is due to the preponderance of the connective tissue after the destruction of the secretory hepatic parenchyma; it is impossible to demonstrate any actual new-growth of connective tissue.

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[1] Compare loc. cit., S. 270, Nr. 26: "In the meso-colon of the sigmoid flexure there were observed thick, white, radiating bands, like those of a cicatrix, which compressed a portion of the veins passing through them;" and S. 273, Nr. 28: the coats of a portion of the small intestine, three feet in length, were thickened, "the corresponding portion of the mesentery was indurated like a tendon."

The color of the liver is darker than normal, dependent, however, in its shades upon the quantity of blood contained in it, and upon a pigmentation of the cells that often appears. The presence of fat may produce a clearer tone of colors. The tissue is, upon the whole, exsanguine and dry; it is only upon section of the larger, relatively broad vessels (particularly the central veins) that blood is discharged.

The diminution in size of the hepatic acini, which is commonly striking, depends upon the reduction in volume of the individual hepatic cells. The latter are smaller than normal, and possess sharply-defined walls; their protoplasm is finely granular, and frequently contains—not only in the vicinity of the central veins, but also throughout the entire acinus—brown or brown-red pigment granules, which are probably formed from the coloring matter of the bile (brown or pigment atrophy, Klebs).

In the gall-ducts no changes are perceptible.

The *symptoms* of simple atrophy of the liver are a slow diminution in the volume of the organ, and the deficiency of bile in the intestinal excretions. The former may be recognized by a uniform diminution of all the diameters of hepatic dulness, and does not affect the left lobe to a greater degree than the right, as in cirrhosis; the dulness in the middle line is, therefore, still perceptible even when that in the mammary and axillary line has already considerably diminished in extent.[1] The diminution takes place so gradually, that its progress will be noticeable only when repeated examinations are made from month to month, or at still longer intervals.

The intestinal excretions present, consequently upon the progressively diminishing secretion of bile, an abnormally clear color, and may at last appear as pale and clayish as when there is some mechanical impediment to the outflow of bile into the intestine.

Frerichs maintains that the clinical features of simple atrophy of the liver are made up of many other symptoms, which he

[1] Compare *Frerichs*, Observ. Nr. 23: Lin. axill., 5 ctm.; lin. pap., 3 ctm.; lin. med., 2 ctm.—*Bertog*, Observ. 1: Lin. axill. and lin. pap., 3 ctm.; by side of the sternum, 2½ ctm. Observ. 2: Lin. axill. and lin. pap., 5 ctm.; lin. stern., 2½ ctm.

attributes in part to the reflex action excited in the system at large by the impaired function of the gland, and in part to the obstruction of the blood of the portal vein. He cites as such symptoms: loss of appetite and a feeling of distention and tightness at the epigastrium, with tongue sometimes clear, and at other times furred; alternation of constipation and diarrhœa, or persistent and profuse diarrhœa, the bowels being regular in exceptional cases only; pale, cachectic appearance, without any jaundiced tinge; wasting of the musculature; as a general rule, accumulations of water in the peritoneal sac, to which general dropsy is soon superadded. But all these symptoms may be absent, as was the case with two patients observed by me suffering from senile marasmus, and where they were met with in the observations communicated by others it is, at least, very questionable whether they are to be attributed to the atrophy of the liver, and not much rather to those changes from which the latter proceeds. This remark is applicable to the loss of appetite and the other signs of impaired gastric digestion in cases where the disease arises in the course of carcinoma ventriculi (Frerichs, Observ. No. 23), or of stenosis of the pylorus (Bertog, Observ. 2); to the exhausting diarrhœa, where this supervenes in ulceration of the bowels (Frerichs, Observ. Nr. 27, 28), or in chronic intestinal catarrh due to compression of the mesenteric veins (Bertrog, Observ. 1). In the absence of any idiopathic affection of the stomach, or of a disease of the bowels not proceeding from the atrophy of the liver, then, even if the wasting of the gland is already far advanced, the appetite may still be good (Bertog, Observ. 1), the stools constantly firm (Frerichs, Observ. 23, 26; Bertog, Observ. 2). That simple atrophy of the liver may give rise to an obstruction of the blood of the portal vein is, indeed, *à priori* improbable. For, although a portion of the capillary vessels is destroyed, along with the hepatic cells, still, the supply of blood in the liver does not necessarily become thereby insufficient, because the entire quantity of blood is also diminished to an extent corresponding to the general deranged nutrition. And, in fact, the ascites is occasionally absent notwithstanding the existence of considerable atrophy (Frerichs, Observ. Nr. 23, 27; Bertog, Observ. 2); still, as a general rule,

it is present, not making its appearance, however, until after the œdema of the lower extremities (Cohn, l. c.; Ruehle, l. c.; Frerichs, Observ. Nr. 28; Bertrog, Observ. 1), and proves, consequently, a concomitant of general dropsy, as is illustrated, furthermore, by the experience of Cohn, that when the effusion is evacuated by means of puncture, its recurrence follows at a comparatively later period than when it has originated from obstruction of the portal vein; but where, as in some of Frerichs' cases, it precedes the anasarca, there are formed, in addition to the atrophy of the liver, changes which tend to produce an obstruction of blood in the portal vein or in its radicles, as, for example, in Nr. 24, occlusion of numerous hepatic capillaries consequent upon melanæmia; in Nr. 36, cicatricial bands in the meso-colon, which compress a portion of the veins passing through it, etc. That the progressive functional derangement of the gland, associated with the atrophy of the liver, is not without detrimental influence upon the condition of the blood, upon the gastric digestion, and upon still other factors of the general nutrition, may be considered as indisputable: wherein, however, this influence consists we are unable to determine; and inasmuch as in all cases serious derangements make their appearance also in other organs simultaneously with the hepatic affection, or even previously thereto, entailing likewise wasting of the body and cachexia, we are, therefore, unable to define more accurately the part played by the hepatic affection in the production of this condition, nor can we even trace to it with certainty the dropsy, particularly as there are cases which run their course without any indication of dropsy.

Bertog observed in his two cases "a quite peculiar, dark-yellow, often decidedly red coloring" of the *urine*, which was exhibited even when voided in very great quantity; that is to say, when it was not concentrated. In one of these cases there was formed, upon the addition of nitric acid containing some nitrous acid, a bluish ring; but not the familiar succession of colors seen in the reaction of the bile-pigment. Even Frerichs found in some cases "a peculiar, hyacinth-red color" of the urine, without being able to detect therein bile-pigment. Inasmuch, however, as, according to the Observations of the last-

named author, the urine is, as a general rule, pale, it remains therefore questionable, whether that peculiar color occasionally met with is especially connected with the atrophy of the liver. Cohn found the color solid brown, and rich in free uric acid, visible under the microscope. The presence of this secretion is so far from constant that, to say the least, no uniform influence of the wasting of the liver upon it is to be admitted.

The *course* of simple atrophy of the liver is invariably chronic. Its *duration* cannot be accurately stated, because the wasting of the gland begins imperceptibly. Starting from the period when its presence can be determined by physical examination, a half-year may elapse, as is shown by Observ. 1 of Bertog, before death ensues. That no mode of termination other than that of death, such as, possibly, an arrest of the process, occurs, is rendered evident by the nature of the causative factors, which are invariably of such a nature as to give rise to severe derangements, not only in the liver, but also even in other organs, as a result of which the fatal termination is never due directly to the hepatic affection alone.

The *diagnosis* of simple atrophy of the liver may be considered as well founded when, in a marantic individual, a quite gradually progressive reduction in the volume of the organ can be made out, which cannot be attributed either to obstruction in the hepatic veins or to cirrhosis, and when at the same time the bilious coloration of the intestinal excreta is abnormally slight, and no indications of retention of bile (icterus of the skin, bile-pigment in the urine) are present. An examination of the thoracic organs will readily prevent our confounding the affection with cyanotic atrophy. It may, on the other hand, be difficult to distinguish it from cirrhosis when ascites is coexistent. Here it is important that, in cirrhosis, the ascites, and that, in simple atrophy, as a general rule, the anasarca of the lower extremities, should form the first dropsical symptom, as well as that the tumor of the spleen should usually be absent in simple atrophy, but present in cirrhosis. Moreover, when the liver is not forced forward, the fact already above referred to, that in simple atrophy the wasting does not affect chiefly the left lobe, may also afford a guide for the differential diagnosis.

The hepatic affection in question is susceptible of *treatment* only in so far that it is our duty to attempt, by prescribing an appropriate dietetic regimen, and by the administration of strengthening medicines—Cohn found the preparations of iron especially efficacious—to check in its progress the marasmus. This object is only imperfectly and temporarily attained in the most favorable cases, because changes invariably lie at the foundation of the general derangement of nutrition leading to the wasting of the liver, against which medical skill proves powerless.

Hypertrophy of the Liver.

Frerichs, Klinik. Bd. 2, S. 200 ff.—*Klebs*, Handb. S. 370 ff., 378 ff.—*Rindfleisch*, Lehrb. 4. Aufl., S. 398 ff.

By the old authors[1] the most diverse affections of the liver, in which the organ presents a uniform enlargement or very striking anomalies of structure, have been termed hypertrophy of the liver; and even up to the latest time, cases are described under this designation where, owing to imperfect or unsatisfactory examination of the finer structural relations, the claim to this title appears at least doubtful.[2]

By hypertrophy of the liver, is understood that enlargement of the organ which is brought about by an increase in the size or the number of the secreting cells. It is obvious that the remaining tissues entering into the structure of the gland, particularly the intra-acinous blood-, lymph-, and bile-vessels, must at the same time be also increased to a corresponding extent: the latter, however, has not as yet been directly observed; and the anatomical diagnosis of hypertrophy of the liver is for the present based upon the evidence, that a simple increase in the volume of the hepatic cells, not due to infiltration or degeneration—simple hypertrophy—or that an increase in their number—hyperplasia, numerical hypertrophy—has taken place. In the former the acini are uniformly enlarged; in the latter this is not

[1] For the literature of the subject, vide *Frerichs*, l. c.

[2] Compare, for instance, *Blachez*, l'Union médic. 1865. No. 92.

necessarily the case. The numerical hypertrophy may also be produced by the circumstance that, through the more abundant development of the trunk of the hepatic vein with its surrounding glandular substance, the number of the acini is increased (Klebs). A strict line of division between hyperplasia and simple hypertrophy of the liver cannot always be sharply drawn, because both processes are progressing side by side.

The cause of the increased nutrition and new-formation of the hepatic parenchyma is, in all probability, to be sought in an increased activity of the glandular cells. The conditions under which the liver becomes hypertrophied, tend in part to favor decidedly this theory.

Where numerous smaller or isolated larger portions of the gland have been destroyed, in consequence of the proliferation and retraction of the interstitial tissue of its specific structural elements, there occasionally ensues a *compensatory* hypertrophy of the remaining sections. Thus, in many cases of cirrhosis, and still more frequently in syphilitic lobulation, the remaining portions of the parenchyma preserved between the cicatricial tissue are seen to be considerably swollen, in consequence of which they project the more prominently beyond the retracted cicatricial spots, and the secreting cells therein contained are enlarged to double and threefold their normal dimensions. To compensatory hyperplasia is it, furthermore, due that, along with a large echinococcus tumor in the principal lobe, or extensive destruction of the same from carcinoma or abscess, the other lobe is unusually enlarged, while its texture is perfectly normal.

A pure diffuse hyperplasia of the liver associated with polycholia occurs, according to Klebs, in full-grown, generally vigorous men, especially *topers*. "The organ is uniformly enlarged in all dimensions, the serous coating smooth and tightly stretched; the weight considerably increased; in the gall-ducts is usually found a very abundant dark secretion. Upon section, the entire parenchyma appears colored dark brown, or, if the quantity of blood is abundant, more bluish. The outline of the lobules is only perceptible upon close observation, but is then quite distinct, the separate lobules appearing small and increased in

number. The hepatic cells have, upon the whole, their normal size."

Simple hypertrophy of the glandular parenchyma not unfrequently occurs in *diabetes mellitus*, where it is probably connected with an increased and accelerated formation of glycogen in the hepatic cells. According to the description of Klebs, the diabetic liver is uniformly enlarged, with somewhat blunt edges, and the consistence nearly normal, possibly somewhat softer than usual. The swelling is to be attributed in part only to the increased quantity of blood, but much more to the enlargement of the glandular cells themselves, whose angles project less sharply, the protoplasm being very abundant and slightly cloudy, the nuclei large and distinct. Upon the application of a comparatively weak solution of iodine, all the cells (according to Rindfleisch, merely the nucleus) become tinged wine-red. Observations of Stockvis and Frerichs show, however, that the swelling of the liver in diabetes may be also due to proliferation or new-formation of the secreting cells. Frerichs found in one case essentially the same alterations as are ascribed by Klebs to pure diffuse hyperplasia (*vide* above).

An occasionally mere hypertrophic, but usually hyperplastic increase of the hepatic cells is the chief cause of the *leucæmic* (and the pseudo-leucæmic) hepatic tumor. The acini become here very large, and the enlargement of the entire organ is often very remarkable, in consequence of which the weight may amount to from four to five, and even from eight to fourteen pounds.[1] So far as we are acquainted with the pathological processes in leucæmia, there is nothing to indicate that the liver here becomes hypertrophied in consequence of the increased functional activity of its secreting cells. Klebs conjectures that the cause thereof may have proceeded from the supply of a more abundant nutritive material from the spleen and the lymphatic glands. The theory is more probable, however, that the same influences which tend to put the spleen, the lymphatic glands, and the bone-marrow into a condition of hyperplasia, may directly give rise also to an analogous process in the liver. Upon post-

[1] *Virchow*, Die krankh. Geschwülste. Bd. 2, S. 570.

mortem examination of leucæmic patients, in addition to the hypertrophy of the liver, the indications of a diminished biliary secretion are not unfrequently met with ; this diminution probably proceeds, however, not from the hypertrophy, but from the secondary alterations of the parenchyma: in a case[1] reported by Frerichs, where the intestine contained a mass completely destitute of bile, the hepatic cells exhibited a highly granular cloudiness of their contents (parenchymatous degeneration).

By the term hypertrophy is usually designated also the enlargement of the liver, which almost invariably makes its appearance in Europeans who have emigrated to *hot climates*, after a shorter or longer residence therein, as is learned from the reports of physicians[2] there settled. Although this idea seems to be favored by the circumstance, that under the same conditions a striking increase of the biliary secretion is observed,[3] yet histological proof is wanting that the questionable enlargement of the organ is in reality due to an increase in the number or size of the glandular cells, and, possibly, not to mere chronic hyperæmia. The same remark is applicable to the hypertrophy of the liver which is said to be produced under the influence of malaria.

There is now and then found, upon post-mortem examination, a liver unusually large and studded with hypertrophied lobules and large secreting cells, without any definite cause, or signs of functional derangement having been known to exist during life (Frerichs).

In the patient the enlargement of the liver due to hypertrophy is frequently only to be determined by percussion, as the resistance of the organ is wont to be perceptibly increased only in the higher grades of hypertrophic swelling. The enlargement which, as a general rule, progresses slowly, is of itself painless. Diffuse hypertrophy of the liver may be diagnosticated, when in one of those affections in which, according to our experience, it occurs, the organ presents more or less enlargement without essential

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[1] Virchow's Arch. Bd. 12, S. 37.

[2] *Le Vacher*, Guide médic. des Antilles, p. 212. *Haspel*, Maladies de l'Algérie. T. I., p. 23. *Heymann*, Verfolgen der phys.-med. Ges. zu Würzburg. Bd. 5, S. 40.

[3] *Hirsch*, Handb. d. hist.-geogr. Pathol. Bd. 2, S. 307.

deviation from its normal form, and when other pathological processes, which, likewise, make their appearance in those diseases, and are accompanied by similar alterations in the physical condition of the organ (such as fatty degeneration, amyloid degeneration, interstitial hepatitis), can be excluded.

PATHOLOGICAL ANATOMY

OF

CANCER OF THE LIVER.

SCHUEPPEL.

PATHOLOGICAL ANATOMY OF CANCER OF THE LIVER.

THE liver should undoubtedly be classed among those organs which have become known as the seat by predilection of many kinds of tumors, especially of those which proliferate and depend upon the formation of new tissue. But if, from an anatomical as well as from a clinico-practical point of view, we take a survey of the entire list of formations of this nature which thus far have been discovered in the liver, it at once appears that medical interest—in spite of the great diversity of the questionable forms of tumors in their anatomo-histological relations—concentrates itself almost exclusively upon a single category, namely, upon the somewhat motley group which has been thrown together under the generic name of *cancer of the liver*. There is of course good reason for this, for, by the term carcinoma, the practitioner promiscuously covers all malignant new-formations; that is to say, all succulent growths which are rich in cells, which develop rapidly, which are seriously prejudicial to the organ invaded, and which not only threaten, but, for the most part, after a brief period, destroy life. The differences in the anatomical peculiarities, and in the minute structure of the neoplasms which are here grouped together under one name, are, in truth, as great as the similarity which they present to the physician at the bedside; for their rapid course and ever-increasing deadliness are elements which belong in common to all the cases of this category. At the same time the physician is able, with more or less certainty, to diagnosticate these growths, sooner or later, both with reference to their probable seat and to their essential (malignant) nature. On the other hand, those formations which lie outside the

term carcinoma in its widest sense—as, for example, tubercle, syphilitic tumors, simple, non-parasitic cysts, cavernous angiomata, certain lymphatic growths, etc.—either do not give rise to symptoms during life (being, therefore, either not susceptible of diagnosis, or their existence being determinable only with a certain degree of probability), or they manifest their benign character by their indolent course, stationary character, final disappearance, or relatively small size.

As a matter of fact, and in contradistinction to malignant formations in the liver, they are only very exceptionally objects of observation and diagnosis at the bedside. In the sense just now expressed, new-formations of a very different nature are classed together under the category of *carcinoma of the liver*. In order to obtain a general survey, and bring a certain order into this complex series, the collective term "carcinoma of the liver" must be separated into its component parts. We cannot make a strictly scientific classification, because the requisite data are lacking, but must remain satisfied with such a division as will meet the practical necessities of the case. With this end in view the groups which are formed must be as nearly natural as possible; that is to say, they must comprise the growths which genetically belong together. We think this may be accomplished by dividing carcinoma of the liver, in its broadest sense, into the following five groups:

1. *Primary* Cancer of the Liver.
2. *Secondary* (metastatic) Cancer of the Liver.
3. Adenoma of the Liver.
4. The so-called *Pigmentary Cancer* of the Liver (melano-sarcoma).
5. Sarcoma and related Forms from the Group of Connective Substances.

In passing we have only to remark that, following Waldeyer, we include under the term cancer those new-formations which depend upon an atypic growth of true epithelium (the skin, mucous membrane, and the so-called true glands); while, with Virchow, we designate by the term sarcoma those tumors which *originate in one of the tissues belonging to the group of connective substances by proliferation and growth of cells, at the expense of the inter-cellular substance.*

1. *Primary Cancer of the Liver.*

The statements of authors in reference to the relative frequency of primary and secondary hepatic cancer differ widely, and are, indeed, diametrically opposed. The further we go back into the past, the oftener do we meet with the assertion that primary cancer of the liver is the more frequent form. But the nearer we come to the present time, so much the more surely in the minds of anatomists than with clinicians does the opinion gain ground that this form is of relatively rare occurrence. Exact estimates of this relative frequency cannot, at present, be given, for it is evident that those who have interested themselves in this problem have, as to the object of their observation and statistics, entered upon the task from different standpoints.

There are two especially characteristic forms under which we meet primary cancer of the liver, viz.: either as a large, *solitary* rounded tumor, which often destroys more than one-half the liver, or as a somewhat uniform, diffuse, cancerous degeneration of the entire organ, the liver meanwhile retaining its original normal shape. In both cases, as a rule, only the liver itself is affected; that is to say, primary cancer of the liver is not metastatic; it extends, at most, only to the neighboring structures, especially to the biliary passages.

It must be admitted that primary hepatic cancer occasionally occurs in the form of *multiple* nodes, similar in size and in other characteristics, but that each node arises independently of the others, or that *one* node represents the primary centre of disease, and has caused the formation of the remaining nodes. So far as the gross appearance of the cancerous masses is concerned, the description which will be given of secondary cancer of the liver will likewise apply to cases of this nature.

If primary cancer of the liver develop as a solitary tumor,[1] the new-growth will be found to be of a somewhat spherical shape, and frequently of enormous dimensions. Sooner or later the tumor makes its appearance on the surface of the liver as a round, irregular prominence, over which the serous envelope becomes thickened and opaque from inflammation. In this locality adhesive peritonitis is occasionally set up, thus preparing the way for

[1] See *Wulff*, Der Primäre Leberkrebs. Diss.-Inaug. Tübingen, 1876.

the extension of the disease to neighboring organs. If such a node is cut through the centre, it generally appears as a soft, tumefied mass, of a dirty white color, pressing above the plane of the incision, and bounded by hepatic tissue, with especial distinctness in those places which are exposed to compression. If the flat of the blade be passed across the cut surface of the tumor, a thick, creamy juice will be pressed out in considerable quantity. Coarser and finer fibres, shining like tendons, are distributed throughout the tumefied, pulpy mass; these fibres are reticular in arrangement, and naturally give the cut surface a very irregular, lobulated appearance. If we attempt carefully to follow the line of demarcation between cancerous and hepatic tissue, it will be observed that the tumor develops in a variety of ways. In many places the whitish, cancerous substance entrenches with a sharply marked border upon the brownish tissue of the liver. The hepatic tissue is not only visibly compressed, but, at the same time, appears to be crowded forward by the new-growth. In other localities, on the contrary, the border-line between cancerous and hepatic tissue is either indistinct or obliterated. The transition from one to the other is effected by means of the hepatic lobules, which swell, become softer and paler, and thus gradually assume the aspect of the mature carcinoma, with which they soon coalesce. Such swollen and fading islets of hepatic substance, which are evidently in a condition of cancerous degeneration, are likewise seen, here and there, surrounded by the normal tissue of the organ, at a distance from the periphery of the tumor. They develop into small nodules, and at a later stage unite with the main growth.

The new-formation readily breaks into the veins. Cancerous thrombi appear in the branches of the portal vein as well as in the hepatic veins, in the latter perhaps more frequently than in the former. Originally they lie loosely within the vessel, but afterward become firmly joined to the vascular walls. The veins which are filled with these cancerous masses are also seen to be greatly dilated. On the other hand, the bile-ducts are compressed and made impermeable by the new-growth, and the larger gall-ducts are occasionally found to be filled by an eruption of cancerous masses. The degeneration may likewise extend to

the lymphatic glands in the fissures of the liver, but primary cancer of the liver usually confines itself strictly to the organ itself. Metastatic affections of distant localities are only exceptional.[1]

The growth of the tumor goes on uninterruptedly until the death of the patient. Meanwhile the morbid formation undergoes a variety of disturbances in its nutrition and circulation, whereby certain retrogressive changes are developed. In the centre of the growth large tracts become necrosed and transformed into a dry, compact, cheesy substance, of a pale, grayish-yellow color; or hemorrhages occur in the tumor, and hemorrhagic infarctions are formed, which likewise undergo simple necrosis, and afterward present themselves as hard, dry masses, of a dirty grayish-red to yellow color. But the most common change is the fatty degeneration of the cancer-cells, which may occur to a greater or less degree throughout nearly the whole of the tumor. In many places it leads to a complete dissolution of the cells, only a fatty detritus remaining; so that, with the exception of its outermost layers, the entire tumor assumes a pale yellow color and a greasy consistency. The cheesy, fatty, and other products of the disturbances of nutrition mentioned, remain unchanged in their place of origin.

The proportion of the liver which is left undisturbed by the cancerous growth is hardly one-half of the original mass of the organ, sometimes even less than this. The normal liver tissue sometimes encloses the tumor as a thin covering; sometimes again it appears to be merely an appendage of the growth. Occasionally the hepatic tissue exhibits its original normal condition, but more frequently it bears the traces of the compression to which it has been subjected by the tumor. Disturbances in the circulation (either anæmia or passive congestion) may also become developed. Finally, the flow of bile becomes obstructed in the normal portion of the liver as a consequence of compression of the bile-ducts, imparting to the organ a yellow, deepening into a greenish, hue.

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[1] See the case of *Weigert*, which is also instructive in other particulars, in Virchow's Archiv. LXVII. S. 500.

Diffuse cancerous degeneration of the liver[1]—the second form under which primary hepatic cancer presents itself—is generally designated as *infiltrated carcinoma* of the *liver*. It is only rarely observed, but appears in a highly characteristic form. The liver is markedly but nearly uniformly enlarged in all directions, perhaps to twice its original dimensions. The external shape of the organ in its coarser outlines remains unchanged. Its serous envelope is rather uniformly cloudy, and somewhat thickened; in places loose adhesions with neighboring organs occur. The outer surface of the liver is covered throughout with slight rounded elevations, whose diameter varies from that of a pea to a small cherry. The serous coat is retracted between these elevations. When the organ is examined externally, it would therefore create the impression that the liver is granular but for the fact that the elevations on its outer surface are larger and have a paler color than in the condition just named.

Even the appearance of the cut surface involuntarily reminds one of cirrhosis, for it is composed of lobules averaging from twice to four times the diameter of a normal hepatic lobule. The lobules are separated from each other by broad ribbons of firm, tendinous, fibrous tissue, and project above the plane of the cut as soft, swelling masses, while the interlobular fibrous tissue appears to be correspondingly depressed. The original hue of the liver has almost entirely disappeared, for the lobules have either a whitish color, or have assumed a yellowish, approaching a greenish tint, from imbibition of bile. Their tissue is looser, more succulent, and more pulpy than that of the normal liver. The inter-acinous septa of fibrous tissue, which *per se* are white, acquire a hue verging from rose to bright red when the organ is markedly vascular, so that the cut surface presents a richly colored appearance. In isolated instances the hepatic tissue has almost entirely disappeared, and traces can only be discovered here and there, with the aid of the microscope. The liver, as such, has vanished, and has been replaced by a cancerous mass of similar shape; every hepatic acinus has been replaced by one of

[1] See Beiträge zur Histogenese des Leberkrebses. *B. Fetzer*, Inaug. Diss., Tübingen, 1868. *Perls*, in Virchow's Archiv, 56. Bd., S. 448, and Virchow's Lehrbuch d. allgem. Pathol., S. 482.

cancer. From the cut surface of such a liver, the same creamy cancer-juice may be expressed that issues from the ordinary cancerous nodes. The cancerous lobules, which have been thus compressed, exhibit, under a magnifying-glass, a spongy or fine reticular structure.

In the form of carcinoma under discussion, retrogressive changes either do not occur at all, or they confine themselves to a partial fatty degeneration of the cancer-cells, whereby the general aspect of the liver is in nowise perceptibly changed.

In individual cases the cancerous infiltration also extends to the parietes of the gall-bladder, transforming them into a firm, whitish mass of the thickness of a finger. In diffuse cancerous degeneration of the liver, the portal vein, as well as the hepatic veins, does not appear to be involved, and, so far as the naked eye can discover, the same may be said of the bile-ducts. Metastases to distant organs, so far as I know, have not been observed; at the utmost the cancerous degeneration affects the lymphatic glands which lie in the portal fissure.

Histology of Primary Cancer of the Liver.—In its minute structure, fully developed primary hepatic carcinoma offers no noteworthy deviation from the ordinary appearances of soft cancer. In general it is very rich in cells, and the framework of fibrous tissue is not well developed in comparison to the former. Its alveoli are commonly large and wide, and nearly round in shape. For the greater part the trabeculæ of the stroma are small, and occasionally are composed almost entirely of naked vessels. In certain cases the cells of this form of cancer have no particular shape or uniform arrangement. But in other cases they possess the form of short cylinders, and, at the borders of the alveoli, at least, are placed beside each other in the symmetrical order of glandular epithelium. On the average the cells of this form of cancer may be said to be small, and their outlines are frequently seen with difficulty; at first they look like a granular ball, similar in shape to the corresponding alveolus, and in which apparently a number of large nuclei are imbedded. That which is said further on, in regard to the blood-vessels of secondary hepatic cancer, will also apply here to the vessels which are distributed in the stroma; the vascular system

of primary cancer of the liver is fed by the hepatic artery; it consists of capillaries which have formed *de novo* within the stroma, *pari passu* with the development of the cancer.

The history of the development of primary cancer of the liver[1] is better known than that of the secondary formation, and is based upon more direct observation. The border-line between hepatic and mature cancerous tissue being much broader and less abrupt in primary than in secondary carcinoma, the former offers for microscopic examination this advantage, namely, that we can more easily observe the processes of development at the periphery of the new-formation, and can form a better judgment concerning them than in the secondary neoplasm, in which, as a rule, the two territories—cancer and hepatic tissue—are almost immediately in contact. The result of the examinations which thus far have been made may be concisely stated as follows: the cells of primary cancer of the liver are to be considered as the offspring, partly of the secretory glandular cells of the liver, partly of the epithelial cells of the smaller bile-ducts. In subordinate questions, the views of various observers are indeed divergent, especially in relation to the extent of the activity which they ascribe to the hepatic cells (or to the epithelium of the biliary ducts) in the production of cancer-cells. In the cases which I have examined, it was almost exclusively the hepatic cells themselves which, by their limitless proliferation, led to the formation of cancer.

That, in other cases, the epithelium of the biliary ducts assume the same rôle, either completely or by preference, is, according to all experience, not only highly probable, but has been positively proven by authentic observers. For that reason it cannot be doubted that there are also mixed cases in which both kinds of cells share the work of cell-proliferation.

In the production of primary cancerous tumors of the liver the events in the cancerous transformation are the same as in diffuse cancerous degeneration of the organ, and, with the help of the microscope, we can observe how these changes are accomplished. The first noticeable event is an enlargement of the

[1] Vide op. cit. of *Fetzer*, *Perls*, *Wulff*, and others.

hepatic cells, by means of which the rows of cells become notably broader. The radiating rows of cells disjoin themselves from their lateral neighbors, because the transverse connecting-links between these series of cells become contracted. The contours of the enlarged hepatic cells become indistinct, or are even altogether lost. The entire structure of the liver seems to have changed into a uniform mass of protoplasm, with a corresponding number of nuclei. In this mass of cells an increase (by fission) of the previously existing nuclei occurs to from twice to four times their original number. The protoplasm gathers about the young nuclei, and new, but somewhat indistinct boundary-lines appear between these multiplied cells. At the same time the young cells assume such an arrangement that, like the epithelial cells of a glandular canal, they appear in the form of a circle around a central lumen. But the process does not stop here. The increase of cells very soon proceeds in an *atypical* manner, and, where previously a row of hepatic cells was seen surrounded by capillaries, we now notice a broad, rounded, egg-shaped or cylindrical alveolus, filled by a mass of cells of darkly granular appearance.

During this transformation the capillaries of the portal system disappear, and the empty capillaries, with the connective tissue which has heretofore surrounded them, form the groundwork of the fibrous trabeculæ of the cancerous stroma. The blood-vessels, which are distributed to the latter and nourish the cancer-tissue, are the products of a new-formation, and are offshoots of the hepatic artery.

In the process here described it is always found that only a small number of the rows of hepatic cells are subjected to the cancerous transformation. The greater portion of the hepatic tissue (the glandular cells as well as the capillaries) undergo atrophy from the pressure of the growing cancer. The same may be said of the smallest of the interlobular bile-ducts whose epithelium, moreover, contributes, within certain limits, to the proliferation of the cancer-cells.

It is difficult to determine the relationship that the cirrhotic growth of the inter-acinous connective tissue bears to the formation of cancer in diffuse cancerous degeneration. This interstitial

growth does not appear to be an independent process, nor does the cancerous degeneration seem to have become connected accidentally and secondarily with an interstitial hepatitis. It is far more probable that the proliferation of the inter-acinous connective tissue forms part of the process of cancerous transformation, since one and the same cause incites the secretory glandular cells to atypic increase, through repeated division, and causes proliferation of the connective tissue after the manner of a chronic inflammatory process.[1]

2. *Secondary Cancer of the Liver.*

In by far the greater number of cases of cancer of the liver, we have to deal with a secondary metastatic formation. The lungs and the liver are the organs in which metastatic tumors of a cancerous, as well as a sarcomatous nature, develop with especial frequency. But hepatic metastases of this nature do not start with equal frequency from every seat of primary cancer, although it would hardly be affirmed of any one organ that the primary cancer which may have been observed therein never furnishes the starting-point for the formation of cancerous metastases in the liver. Metastases in the liver occur most rarely from carcinoma of the skin—the true epithelial cancer; and, when this does take place, the metastatic nodes remain small and quite isolated. On the contrary, secondary cancer of the liver oftenest follows primary cancer of the stomach, especially of the pylorus; likewise proceeds from carcinoma of the intestines, and from the cancer of the peritoneum connected therewith. This fact at present seems perfectly intelligible, since we assume a transportation of cancer-germs from the stomach and intestines to the liver, through the medium of the portal vein and its radicles, or by means of the lymphatics. The readily-observed fact that the younger, secondary cancer of the liver usually grows much more

[1] To this problematic condition of the liver *Perls* (Lehrbuch d. allg. Pathol., S. 482) has given the name of *cirrhosis hepatis carcinomatosa;* but I am unable clearly to distinguish in what manner he explains the connection of the phenomena. Apparently he sees nothing which is accidental in the cirrhosis of the connective tissue, but considers it an element of the general process.

rapidly and luxuriantly—and therefore more quickly reaches a greater size, and also, to a larger extent, reveals the signs of retrogressive changes—than the older, primary cancer whose seat is in the pylorus or intestines, is of the greatest importance in judging of the relations which here come in question; for the cancer last named is sometimes of such limited extent that it might be quite overlooked by a negligent observer. Its development ceases at an early period, or a destruction of the primary cancer occurs, and only a more or less characteristic cicatrix remains behind. Since in some cases the primarily-diseased organ causes no decided symptoms, we can easily understand why it is that the imposing carcinomatous growth in the liver leads one, *intra vitam*, to overlook the actual place of origin of the lesion, and that, even post-mortem, it is discovered only by a careful and systematic examination. In such a condition of things, we would hardly venture to consider the insignificant cancer of the pylorus as primary, and the immensely developed tumor of the liver as the secondary disease, if we did not succeed in discovering, here and there, the road over which the cancer-germs had travelled, and if numerous veins and lymphatics, filled with cancer-juice, did not point out the direction in which the spread of the disease has occurred. In many cases we can only conjecture the relation of these changes, and make a diagnosis only by analogy; again, in others the question cannot be answered at all. For the most part, however, in a simultaneous occurrence of cancerous nodes, on the one hand in the liver, and on the other in some other organ, especially when the latter lies within the compass of the portal system of veins, the assumption is warranted that the hepatic cancer is the *secondary* and *younger* formation, even when it is of far larger growth, and exhibits more extensive retrogressive changes, than the cancerous nodes which exist elsewhere, and of which *one* is the primary and older formation.

Secondary carcinoma of the liver appears, almost without exception, in the form of *multiple nodes*, and only with extreme rarity as a diffuse infiltration.[1] In many cases, the liver having

[1] In a case of colloid cancer of the liver, I have seen diffuse infiltration in connection with a corresponding disease of the peritoneum and stomach.

been affected at a relatively late period, the cancerous nodes in the latter are so small and so few in number, that they may be first discovered, and to a certain extent accidentally, in the cadaver. But, commonly, the nodes in the liver attain such a development that they are distinctly perceptible during life. The size, number, and other characteristics of the tumors present the greatest differences. Sometimes, as already mentioned, there is only one, sometimes only a few; again, there are twenty, thirty, or even hundreds of nodes, which are distributed throughout every portion of the liver, without regularity. If the nodes are very numerous, they not only appear on all parts of the surface of the liver, but the organ cannot be cut open without disclosing a number of similar nodes situated deeply within the tissues. The size of the individual nodes differs extremely, not only in different cases, but also in the same case. The largest nodes reach the size of a child's head; on the average, they are about as large as an egg or an apple; but they also occur in every possible dimension, from thence downward to miliary or even smaller size. Individual nodes generally appear to be sharply circumscribed; but, on account of their peculiar (excentric) growth, they cannot be easily detached, and are not really encapsulated, for their borders are immediately in contact with unchanged hepatic tissue. In connection with this excentric growth of the cancer stands the fact that the hepatic substance but seldom exhibits the signs of compression in the neighborhood of the nodes. The hepatic tissue is not even displaced by the cancer, for the latter takes the place of, and is substituted for, the former. Each individual node grows at its periphery, but also increases in size, by gradually coalescing with the smaller nodes in its neighborhood.

The *consistence*, *color*, and *other characteristics* of secondary cancer of the liver are in their essentials in accordance with the nature of the primary cancer, whose peculiarities they repeat even in detail. The cancerous nodes of the liver at one time exhibit the density of scirrhus, at another the softness of medullary cancer. The extremes in both directions are exceptional, for, as a rule, they have a medium consistence (carcinoma simplex). When the knife is drawn across the cut surface of an

incised node, there issues, almost without exception, and always in fresh specimens, a creamy cancer-juice, sometimes in profuse, sometimes in moderate quantity. Very large medullary nodes occasionally give emission to an abundant thick mass of cells, after removing which a coarse, fibrous net-work (stroma) remains, whose meshes are of the size of a millet-seed, while the trabeculæ have the thickness of a hair. In general the cancer nodes of the liver are very succulent; dry nodes form the exception (*e. g.*, epithelioma). All cancer, so far as it has not become retrogressively changed, has either a whitish hue, or a pink, gray, yellow, or greenish tinge, bordering upon white.

Since, in the early stages of their growth, the cancer nodes simply take the place of the hepatic tissue, the liver, at first, experiences no perceptible change in its dimensions. Sometimes the form and volume of the organ are not changed, although it contains a great number of nodes, if the latter do not exceed a given size, *e. g.*, that of a cherry. Gradually, however, as the nodes become more numerous, and especially when certain of them steadily increase in magnitude, the shape, volume, and weight of the liver undergo striking changes. On the surface of the organ the nodes emerge in the form of smoothly rounded elevations, which, as they continue to increase in size, give the liver an uneven and very irregular appearance. The organ enlarges in all its dimensions, especially in thickness, and its weight increases two- or threefold; in some cases a cancerous liver attains a weight of twenty pounds, and upward. The largest and heaviest livers yet observed were cancerous.[1] When the tumors have attained an extreme size, but very little of the hepatic tissue remains. When the liver is studded with nodes of considerable size (as large as a fist), which are almost in contact with each other, the normal hepatic tissue may not amount to one-fifth, or even less, of its original quantity. Decided alterations, as a rule, are not perceptible in the hepatic substance lying between the nodes. As has been already remarked, there are no noticeable effects of compression. Circulatory disturbances occasionally arise in the form of a stasis at the margin of the nodes, whereby

[1] The same may be said of the so-called pigment cancer of the liver (vide below).

a distention of the vessels occurs, and the hepatic substance assumes an almost cavernous aspect. Frequently, however, a certain degree of icterus develops at first in the substance of the liver, and afterward in the cancerous nodes. This arises from the closure of numerous biliary ducts by the pressure of the nodes upon them. This explains the fact, also, that the icteric discoloration is often only partial or maculated.

When the hepatic substance is studded with nodes, similar masses, at the same time, often exist in the walls of the gall-bladder, or in the larger gall-ducts. In most cases we know nothing certain concerning their origin and their relation to the hepatic cancer, since commonly one-half of their circumference is surrounded by hepatic substance, while the other half projects into the lumen of the gall-ducts. The question as to their starting-point loses its significance as soon as we are entitled to assume, from the revelations of the autopsy, that the cancerous formations within the liver are really secondary. If, however, the carcinoma is limited to the liver and biliary passages, we cannot dismiss the possibility that the cancer of the biliary passages (originating in the epithelium of their mucous membrane) was the primary formation, and that the liver was thence infected by cancer-germs. This would be the more probable, according as the cancer of the gall-bladder is larger and its development and retrogressive changes are more pronounced. It is self-evident that the contrary is also *possible*. Even when we study all the peculiarities of the individual case, we cannot attain more than a certain degree of probability in these questions.

In secondary cancer of the liver the blood-vessels of the organ are likewise often involved. Most frequently we find the branches of the portal vein within the liver filled with soft cancerous thrombi. Vessels thus filled with cancer tissue, over larger or smaller tracts, often lose themselves imperceptibly in the cancer nodes of the liver. In these cases, too, it cannot always be determined whether the hepatic nodes first broke into the portal branches, and then developed after the manner of cancer of the veins, or whether a cancer at the portal vein spread over its capillary district to the liver tissue. If, as is not seldom the case, a gastric cancer coexists, and we find the gastric veins

issuing from its neighborhood (as also all the branches of the portal vein) filled with cancerous masses, and, further, if the cancerous thrombi in the smaller hepatic branches of the portal vein are continuous with the carcinoma of the trunk of the portal vein, then we must consider the hepatic nodes, which are confluent with the cancerous thrombi, as a direct continuation of the latter.

The extension of secondary hepatic cancer to the hepatic veins and a continuation of its growth within them, after the manner of cancer of the veins, is a relatively rare occurrence. An invasion of the inferior vena cava by cancerous nodes is perhaps still more rare.

The lymphatic glands, which lie in the portal fissure, are likewise found to be subjects of cancerous degeneration in secondary hepatic cancer. They are converted into tumors of the size of a nut or a hen's egg, and in many instances exert a serious pressure upon the bile-ducts and blood-vessels which enter, and emerge from, the portal fissure.

In the majority of cases no evidences of a participation of the lymphatics in the extension of secondary cancer of the liver can be perceived. (See, however, what is said later in connection with colloid cancer.)

The peritoneal investment of the liver, as a rule, offers a hindrance to the development of cancer in the peritoneum. In rare cases adhesions occur between the surface of the liver and neighboring organs, and extension of the hepatic cancer occurs by means of such adhesions, especially to the transverse colon and the anterior abdominal wall.

While the cancerous nodes of the liver continue to enlarge at their periphery, new tumors, springing up, perhaps, between the old ones, the older portions of these growths suffer every kind of nutritive disturbance; various *retrogressive* changes finally occur, which, in the majority of cases, are due to disturbances or interruptions in the circulation of blood within the vessels of the cancerous stroma. These disturbances arise most readily in localities which are farthest removed from the sources of nutrition. And since the latter lie at the periphery of the nodes, their centres are the first to be affected by the embarrassment in the

circulation. Generally, also, very large tumors of rapid growth show the most pronounced form of retrogressive change. These changes consist chiefly of fatty degeneration, softening, disintegration, and resorption, and they occur first of all in the *cancer-cells* within the alveoli. The cancer-*stroma* may participate in these processes, within certain limits.

In many cases the *fatty degeneration* extends uniformly throughout entire nodes, but affects only the cancer-*cells*, the stroma meanwhile remaining intact. The alveoli are then filled with a fatty detritus, and the degenerated nodes present the color and consistence of butter (buttery cancer).

At other times, if the stroma share extensively in the degeneration, the cancer node is changed into a soft, liquefied, whitish gray mass, which can be washed away by a stream of water like the contents of a spot of softening from cerebral apoplexy.

Generally, however, this process of fatty degeneration and resorption is only partial, and is limited to the oldest portion, *i. e.*, to the centre of the node, and even here attacks only the cancer-cells, leaving the fibrous stroma untouched. By shrinkage the latter retracts into a solid fibrous mass—the so-called *cancer-cicatrix.* In nodes which are situated on the surface of the liver, and in which the shrunken centre of the cicatrix is connected with the peritoneal investment of the organ, the middle of the projecting node becomes indrawn after this process and presents a saucer-shaped depression, thus forming the so-called cancer umbilication. The peritoneum at the bottom is thickened and opaque from inflammation. The umbilication may even be observed in the nodes of moderate dimensions, *i. e.*, the size of a cherry.

As is well known, umbilication is not a peculiarity of hepatic cancer alone. It appears, in an entirely similar manner, in the cancerous nodes of other organs which have a serous investment, if these nodes lie in the vicinity of the serosa, *e. g.*, in cancer of the intestines, of the pleura, etc. Something analogous occurs even in the retracting cancer of the breast, which has formed connections with the skin. On the contrary, in those tumors of the liver, which do not belong to true cancer, in the sense held by us—for example, in metastatic sarcoma, pigment cancer, etc.—umbilication is generally lacking. Some cases of multilocular echinococci of the liver, when they press forward to the serosa, present inequalities which, at least to the palpating finger, suggest umbilication.

The larger cancer nodes, through the retrogressive processes in question, sometimes give rise to the so-called *cystic cancer*, *i. e.*, a node whose centre contains a roundish cavity filled with serum, the walls generally not being entirely smooth. Their origin is due to the disintegration and resorption of the oldest portion of the hitherto solid cancer nodes, serum taking the place of the resorbed tissue. The central cyst, however, is always enclosed in a broad zone of younger cancer tissue.

A species of *cheesy degeneration* is sometimes observed, but is more rare than fatty change with its sequelæ. In individual cases the cheesy change extends over all the tumors present, and involves their entire volume; generally, however, it is limited to isolated districts of the larger nodes. The cancer nodes become dry and hard; and a cut surface assumes a yellowish gray, homogeneous look, which gives the entire node an appearance very similar to a large conglomerate of tubercle, or to an old gummy growth. The cheesy substance is derived principally from the cancer-cells, which become dry and atrophied, and finally die and break up into a finely granular detritus. The cancer-stroma also participates in this process; the circulation in it is arrested, the vessels are destroyed, the stroma dries and becomes necrosed, and in consequence is likewise transformed, at least in part, into a cheesy detritus.

Carcinoma telangiectodes (fungus hæmatodes) is distinguished by an unusually rich development of the finer blood-vessels of the cancerous stroma. These tumors contain, therefore, a large quantity of blood, are of a bright rose-red color, and are very soft; they seem to grow with great rapidity, and very frequently are the seat of smaller or larger extravasations. The hemorrhagic cancer originates in this manner. Entire cancer nodes may be broken up by profuse hemorrhages, and converted into a bloody pulp. If tumors of this nature are situated in the vicinity of the peritoneum, they may tear through the latter, thus allowing the blood to pour into the abdominal cavity. In a case of this nature, I found the blood, which had issued from the cancerous node of the liver, in Douglas's cul-de-sac, exactly like an hæmatocele retro-uterina. Sometimes the rupture of the peritoneum gives rise to an acute peritonitis.

We may also speak of colloid cancer at this point. This form of growth is of rare occurrence in the liver; indeed, it never exists in this organ as a primary growth. Colloid cancers of the liver are partly metastatic (as a consequence of a similar growth in the stomach and intestines), partly an extension from the peritoneum. In the metastatic cases the liver contains a number of nodes, which can be distinctly seen to have originally been ordinary (cellular) cancer. For, besides wide alveoli filled with a homogeneous colloid mass, these tumors contain other alveoli with pure medullary contents, and others again whose cells exhibit the various stages of mucoid degeneration. Aside from this transformation of its cells, the nodular colloid cancer of the liver does not differ in any important particular from ordinary secondary cancer.

The anatomical appearances are quite different when a colloid cancer of the peritoneum advances uninterruptedly to the liver. This takes place principally through the medium of the subserous lymphatics. A number of small lymphatic rootlets, filled with gray, transparent, cancerous colloid, which shines through the walls of the vessels, can be seen under the peritoneal investment of the liver and gall-bladder. The rootlets are connected with a widespread, small-meshed net-work of lymphatics, which are similarly changed and greatly distended. The meshes become closer and narrower, their trabeculæ broader, the interstitial tissue gradually disappears, and thus arise, in and beneath the serous membrane, flat, infiltrated plaques of colloid cancer, constantly increasing in depth, and unceasingly taking the place of the hepatic substance. The colloid growth, however, appears not only on the surface of the liver, but at the same time penetrates into the interior of the organ. When the liver is incised, numerous fine canals and a canalicular net-work filled with colloid matter—the canals are evidently lymphatics—are seen in the connective-tissue sheaths of the larger blood-vessels. These lymphatics pass like strings into the hepatic tissue. At a somewhat later stage the blood-vessels become sheathed in a zone of colloid matter, nearly equal in thickness to their own diameter, and from these the colloid cancer grows at the expense of the hepatic tissue, in the same way as at the surface of the organ.

Finally, without any special change in the shape of the organ, even without any important increase in its size, extensive districts, and perhaps an entire lobe, may be composed exclusively of colloid cancer. The walls of the gall-bladder likewise become involved in the colloid infiltration through the medium of the sub-serous lymphatics. Its mucous membrane may remain free; occasionally, however, the colloid cancer breaks into the cavity of the gall-bladder.

In spite of all the retrogressive changes which have been mentioned, recovery from cancer of the liver can never occur. For some time there was an inclination to believe in the possibility of recovery, on account of an incorrect interpretation of certain post-mortem appearances.[1] This question is so definitely settled at the present time that it seems superfluous to enter anew upon a discussion of the curability of cancer.[2] The various degenerations of cancer of the liver may perhaps protract its course, but never produce its arrest, and still less a true involution. For we can always convince ourselves, by careful observation, that the outermost layer of the cancer nodes consists of unchanged cancerous tissue, and that the peripheral growth is constant, undisturbed by these retrogressive changes which the older portion of the growth experiences.

Secondary carcinomata of the liver repeat, as do cancerous metastases in general, all the histological characteristics of the pre-existing primary tumor, sometimes even in the most minute details.

In accordance with this fact, the cancer nodes of the liver, although agreeing in the general features of their constitution, present, however, manifold deviations from each other, both in regard to the stroma and to the cancer-cells. The connective-tissue stroma is sometimes well developed, and forms almost half of the entire node; sometimes it exists in such small quantity that its blood-vessels seem to course almost nakedly through the soft, pulpy mass of cells, and only a few stronger fibrous

[1] Syphilitic tumors, in a condition of involution, seem especially liable to be mistaken for hepatic cancer in a state of recovery.

[2] See *Koehler*, Krebs- und Scheinkrebskrankheiten. S. 376. *Frerichs*, Klinik der Leberkrankheiten. II., S. 282.

trabeculæ afford support to the latter. The alveoli, in which the cells lie, are at times relatively wide, again narrow and delicate. Their shape, likewise extremely variable, depends, as is well known, more upon the direction in which they have been cut, than upon original differences in form. The *cancer-cells*, the most important factor of the new-formation, present a great variety in their number, shape, size, and arrangement. Their number and arrangement correspond naturally with the character of the stroma. In relation to their shape and size, however, it is to be remembered—according to the definition which we have accepted, that carcinoma is an *epithelial* new-formation—that its cells may therefore present all those forms which the epithelial cells of the most varied sites assume. But, as is well known, the shape of the cells essentially depends upon their respective position, and they must fit into the space appointed to them; each one is obliged to take the place which the others have left for it. For this reason it is often the case that there can be no question of a definite form and arrangement of cells within the alveoli. It is quite otherwise in cases of the so-called cylindrical-cell cancer and the very rare pavement epithelium cancer. We very frequently meet with cylinder-celled carcinoma in the liver, because the primary cancer of the stomach and intestines, which, with especial frequency, is transferred to the liver by metastasis, usually presents exquisite types of this structure. The alveoli of cylinder-celled cancer are generally long and narrow, like the canals of tubular glands. The elongated and equally broad cells stand close to one another, with the long axis perpendicular to the alveolar wall. The free space between the cells in the centre of the alveolus is likewise filled with cells of shape varying from a long oval to caudate, but without systematic arrangement.

The *blood-vessels* of the cancer nodes are supported by the trabeculæ of the stroma, forming a more or less close net-work, generally of a capillary nature. They occur in very diverse number and compactness, and, when largely developed, are usually enclosed in an extremely delicate connective-tissue sheath. For the most part, the finer blood-vessels of the cancer stroma are *newly formed;* this explains their great delicacy and the ease

with which they are torn. According to the researches of Frerichs[1] in this direction—by means of injections—the capillary system of the cancer nodes receives its supply from the hepatic artery. The capillary net-work, which formerly existed in the locality of a node, and was outspread between the branches of the portal vein and the veins of the liver, becomes lost as the cancer develops. Only the larger branches of the portal and hepatic veins course through the nodes; but, unless the cancer breaks into the interior of these vessels, they gradually become compressed and destroyed. The branches of the hepatic artery which nourish the cancer nodes are relatively wide, and in very largely developed carcinoma the trunk of the main artery itself is perceptibly dilated.[2] On the other hand, the branches of the portal vein, which lie in the neighborhood of the cancerous tumor, are compressed, narrowed, and do not admit an injection mass.

Histogenesis.—Histologists have given carcinoma of the liver a certain preference as a starting-point for their researches into the origin of cancer. It may be doubted as to whether this was a happy choice. At any rate, the fact that the majority of observers have made no strict differentiation between primary and secondary cancer, and between cancer and sarcoma of the liver, and that accordingly they have not hitherto agreed concerning the nature of the object of their research, has certainly contributed greatly to the prevailing differences of opinion in regard to the origin of carcinoma of the liver. So far as *secondary hepatic cancer*[3] is concerned, every one who has made a thorough microscopic investigation of the subject will agree with me in the assertion, that the microscope does not give an adequate explanation, either of the genesis of carcinoma of the liver, or of the share which the various tissue elements of the liver have taken in its formation. For, though we examine the very youngest nodule, we learn at most how it *grows*, not how it has originated; nor can we discover what shape it took in the earliest stages of its existence. This hiatus must be filled by supposi-

[1] Klinik der Leberkrankh. II. S. 276.

[2] Vide *Frerichs*, loc. cit.

[3] Cf. the remarks in the remaining sections on carcinoma of the liver.

tions based upon the facts with which our knowledge of the development of cancer has supplied us. The latter processes of growth are likewise difficult to follow microscopically; for the boundary between cancer and hepatic tissue forms a sharp line, on one side of which lies the unchanged, or atrophied, liver substance, while mature cancer tissue already exists on the other side. No gradation between the cells of these two tissues is perceptible. On the contrary, we can see that the connective-tissue trabeculæ of the stroma are the direct continuation of the capillaries, which course between the rows of hepatic cells, together with the sheaths of connective tissue surrounding these vessels. The uniform repetition of this appearance creates the impression that the growth of the secondary cancer nodes is effected by means of a progressive division and increase of the already existing cancer cells at the periphery of the node, during which process the liver-cells remain passive, atrophy, and quickly disappear, while the cancer-stroma represents the remains of the hepatic substance after the destruction of the liver-cells, *i. e.*, the withered capillaries in combination with their accompanying connective tissue. That a new-formation of capillaries, which are nourished by the hepatic artery, takes place in the connective-tissue frame-work of the cancer, is proved, not by means of the microscope, but by "injection experiments." But as regards the earliest steps in the formation of the tumor, as already remarked, we are confined to hypotheses. Our opinion is that the germs of the new-formation have wandered, or have been carried into the liver. This would occur preferably, or even exclusively, through the medium of the blood-vessels and lymphatics. These germs consist of cells which previously were elements of the primary cancer, but have broken off from the growth, and, after reaching the liver, have continued an independent existence. Through repeated division of these contraband germs, a cluster of cancer-cells is formed, and this, by continuous proliferation, sends out shoots and branches in all directions. The latter force themselves into the interstices of the hepatic parenchyma, and take the place of the latter. That the theory of the histogenesis of secondary carcinoma of the liver here presented does not meet with general acceptance, but that individual investigators differ

concerning the chief, as well as the subordinate points of this view, does not require especial remark. Simply because the process of the origin of cancer conceals itself from direct observation, every inquirer thinks himself entitled to fall back upon the theories of cancer which he has previously accepted, and by their help fill the gaps in the observation. Thus it happens that almost all possible methods of origin are accepted; one observer asserted that the cells of secondary cancer are derived from the hepatic cells and the epithelium of the biliary-ducts; while another claims that they originate in the endothelium of the blood-vessels, especially in the endothelial tube of the capillaries; while a third finds their source in the cellular elements of the connective tissue, etc.

3. *Pigment Cancer* (*Carcinoma Melanodes*). *Melano-Sarcoma.*

Until within a short time pigmentary tumors were classed by most authors among the carcinomata whenever they pursued a malignant course. Virchow[1] was the first to emphasize the fact that many of the so-called pigmentary cancers should be included among the sarcomas, and he accordingly termed them melano-sarcoma. If, however, we consider the characteristic of carcinoma to consist in its epithelial origin, while the tumors which are due to proliferation of cells in the tissue belonging to the group of connective-tissue substances, are included under the term sarcoma, we cannot doubt that all pigmentary growths, which do not belong to the benign melanomata of Virchow, must be classed among the melano-sarcomata, and not among carcinomata. For we can readily convince ourselves that the cells of these tumors are not of epithelial origin.[2] We hold, therefore, that the melanotic tumors which are found in the liver are without exception melano-sarcomas in the genetic sense above mentioned. This, however, shall not prevent our use of the convenient

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[1] Krankh. Geschwülste. II., S. 271, et al.

[2] Whoever accepts, on the contrary, the alveolar structure as a criterion of cancer, will consider certain cases of melano-sarcoma (likewise of the liver) among genuine cancer. For it is a matter of fact that there are tumors of this nature with a structure resembling that of cancer, *i. e.*, alveolar.

name of *pigment cancer* for these growths. Pigment cancer occurs with extreme rarity as a *primary* formation in the liver. Many authors have doubted or denied such an event, but, as it appears, without sufficient reason. Isolated observations are opposed to this view. For example, under the name of *primary melanotic endothelioma of the liver*, Block[1] recently described a case of diffuse or infiltrated pigment cancer, which belongs in this category, and in which the primary affection of the liver cannot well be doubted. Frerichs[2] reports an analogous case of spindle-cell sarcoma of the liver with partly pigmented cells; numerous yellowish and blackish nodules, from the size of a hemp-seed to that of a pea, were found in the greatly enlarged liver of a woman fifty years of age.

As a rule, pigment cancer of the liver is due to a process of metastasis. The primary location of the tumor in question, as is well-known, is most frequently in and about the eye, as well as in the skin. If metastases originate from these localities, they may appear in various viscera, but occur with especial preference and frequency in the liver. In no other place does secondary melano-sarcoma approach the exuberance of development, or so rapidly attain such an enormous volume, as in the liver. As in genuine carcinoma, the metastatic disease of the liver in pigment cancer arrives at dimensions in comparison with which the primary nodes sink into insignificance. The liver furnishes without doubt an especially favorable soil for the development of melanotic tumors.

Pigment cancer occurs in the liver, sometimes in the form of multiple nodes (which occasionally present the structure of "radiated sarcoma" ["Strahlenkrebs"[3]]), sometimes in the form of a widespread, diffuse infiltration. Not unfrequently both forms appear to be combined in varying proportions.

In nodular pigment cancer, as in the common forms of carcinoma, we find a large number of rounded tumors in all parts of the liver. The nodes, whose size varies from that of a cherry to that of an apple, or even larger, for the greater part seem to be

[1] Arch. d. Heilk. XVI. 1875. S. 412.

[2] Klin. d. Leberkrankheiten. II., S. 319, et seq.

[3] For further particulars vide p. 349.

sharply circumscribed, but do not appear to be encapsulated. Their color is now a black to blackish brown, now a light or dark gray; again, they are of a varying black spotted with gray or white. Aside from their color, the cut surface of these nodes is homogeneous, their consistence moderately firm, but somewhat softer than the surrounding hepatic tissue. If the knife-blade is carried across an incised node, as a rule, a genuine cancer-juice of creamy consistence does not appear, but only a cloudy serum, intermixed with very small black fragments of the tumor. But when softening and disintegration of the pigmented cells have occurred, pressure causes the flow of a sepia-colored, ink-like fluid, of serous consistence, in which cells, cellular detritus, and, especially, numerous free pigment granules, are suspended. The nodes project from the surface of the liver in a globular shape, but are somewhat flattened. The serous membrane which covers them is smooth and, at the most, is slightly clouded. The peculiar umbilication of genuine cancer nodes is generally lacking in nodular pigment cancer.

Through the presence of these nodes, the liver experiences a considerable increase in circumference and weight. In the cadaver the organ is not unfrequently found to weigh from twelve to fifteen pounds, and in isolated cases attains a weight of twenty and even twenty-five pounds. In spite of this, the hepatic tissue between the nodes may be much reduced in volume. It likewise suffers changes similar to those experienced in genuine hepatic cancer, and it assumes with especial frequency an icteric color from the same causes as in the latter lesion. Certain tracts of the preserved liver tissue, or perhaps its entire extent, often have an irregular brown and grayish black, flea-bitten or granite-like appearance, which is due to the fact that very small groups of pigmented tumor-cells are deposited between the partially normal tissue elements of the liver. This will be described more in detail under Infiltrated Pigment Cancer.

Concerning retrogressive changes—in addition to the more rarely observed hemorrhagic saturation of individual nodes leading to complete destruction, and which, when they occur in the neighborhood of the peritoneum, may cause its rupture, and result in hemorrhages into the abdominal cavity, followed by peri-

tonitis—nothing is worthy of mention, save a degeneration of the nodes into a thick, black, pulpy mass. In this condition the cells of the tumors are converted into a detritus consisting almost entirely of pigment granules. There are no further changes; the detritus remains passive without being resorbed.

The anatomical picture of *diffuse infiltrated pigment cancer*[1] is essentially different from that of the conditions hitherto described. In the lesion in question the liver enlarges very considerably in a relatively short period, and without experiencing a notable change in its external form. Within a few months it reaches a weight of from fifteen to twenty, indeed, even twenty-four pounds. In the later stages of the disease we generally find all parts of the liver, although not to the same degree, undergoing the changes in question. The external surface of the organ, however, generally remains smooth; but in those localities in which the infiltration, with the elements of the pigment cancer, has become very compact and dense, broad, but very flat, knob-like protuberances appear. The capsule of the liver covering them is slightly clouded.

The enlargement of the liver is caused by a deposit of tumor-cells between the normal, formative elements of the organ. In all directions the hepatic cells are so intimately commingled with the cells of the pigment cancer that it is quite impossible for the unaided eye to distinguish the hepatic substance from the new-formation. The hepatic cells remain—in a more or less compressed and atrophied condition—between the cells of the pigment cancer, or they soon become completely destroyed from the growth of the tumor cells. But in both cases the peculiar acinous structure of the liver remains distinctly recognizable. The cut surface of such an organ presents an extremely variegated appearance. The acinous structure may still be recognized in all directions, even in the spots which have suffered the greatest change; the acini, however, are greatly enlarged, and

[1] In an exact acceptation, only a *predominance of node formation or of infiltration* of pigment cancer should be mentioned, because in the former there are almost always infiltrated tracts, and in the latter fully developed nodes may be observed in the centre of the infiltrated portion or near the same.

exhibit a mixed color, which is compounded of the brown of the liver substance and the white and black of the infiltrated new-formation. This parti-color presents all possible shades from brownish black to the palest gray brown; the color also changes according to the extremely variable quantity of blood in the different portions. Small black nodules, more or less distinctly circumscribed, are strewn throughout the diffusely infiltrated tissue, the growths varying in size from a poppy-seed to a small cherry. The smaller ones exist in large numbers. Since, however, the so-called pigment cancer contains not only black cells, but also cells which are either free of pigment, or possess but little, we find white or light gray nodules side by side with the black ones; and in localities in which these colorless cells occur in the nature of an infiltration, the hepatic tissue becomes paler by the admixture of white and light gray. In this way the cut surface of the liver receives a peculiarly spotted or flea-bitten aspect, which has not inaptly been compared to granite, and has led pathologists to bestow upon this questionable formation the name of *granite-like cancer*.

We are aided by few thorough examinations relating to the *finer structure* and histogenesis of *pigment cancer of the liver*. The principal constituents consist of cells which, for the greater part, or even wholly, are pigmented. The pigment is partly dissolved, the cells having a diffuse brown color; partly exists in the form of black granules, which lie embedded in the protoplasm. The pigment granules are often present in such quantity that they conceal everything else, and give the cells the appearance of black, homogeneous masses.

The cells of nodular pigment cancer have a round, elongated, or spindle-shaped form, frequently caudate, and are held together by a small quantity of fibrillated or pulpy-albuminoid connective substance. A definite arrangement of the cells is not always perceptible, especially when they are round in shape. Commonly, however, the cells are spindle-shaped, and lie side by side in small bundles, which are mutually interwoven. The black nodes are rich in delicate, newly-formed blood-vessels. According to the analogy between this growth and hepatic cancer, it is probable that these vessels proceed from the hepatic

artery, while the vessels which are connected with the portal and hepatic veins have been probably destroyed.

With regard to their *genesis*, it is assumed that the individual nodes are produced by the increase of cells which have become loosened from the primary tumor, and have wandered into the liver. There is no direct evidence as to the manner in which this is effected, although it is presumable that the transportation is effected by means of the hepatic artery. When they have reached the liver, these cells increase by a constant proliferation, the liver meanwhile remaining perfectly passive, or rather it seems to become compressed by the growth of the new-formation. In all probability those districts of the organ which previously were unaffected become infected later by the nodes which were first developed.

We are better informed concerning the histogenesis of infiltrated pigment cancer of the liver. I have examined a case in a man forty years of age, who had a melanotic tumor of the choroid,[1] and who died some months after the enucleation of the eyeball. The autopsy revealed an enormously enlarged liver and spleen, both organs being the seat of infiltrated pigment cancer; the remainder of the body, however, was entirely free from metastases. In shape and size the cells of the morbid growth were similar to those of an ordinary mammary cancer, but were pigmented in different degrees. In the spleen they were either isolated or strewn in little groups between the cells of the red pulp. They were likewise intermingled with the blood-corpuscles in the so-called capillary veins of the spleen. In the splenic vein, as well as in the trunk and hepatic branches of the portal vein, a considerable number of morbid cells were lodged, and were easily recognized by the pigment they contained; they were found not only in the blood itself, but likewise in thrombi which existed in the vessels mentioned. In the liver, however, the capillaries of the portal system were almost everywhere crowded with cells of the pigment cancer, and were devoid of blood. The capillaries were notably dilated, the rows of hepatic cells between them being correspondingly compressed and atro-

[1] Arch. d. Heilk. IX. 1868, p. 389 (with microscopical plate).

phied. In the localities which were most abundantly infiltrated the cells of the liver had completely disappeared, the capillaries —filled with morbid cells—were in contact with each other, and, together with the remains of the compressed hepatic substance, formed a frame-work with regular, rounded alveoli, very similar to the connective-tissue stroma of ordinary cancer, and nourished, like the latter, by capillaries which belonged to the hepatic artery. There can be no doubt in this case that the germs of the morbid formation, if not exclusively, still in very large proportion, wandered through the portal vein, starting primarily from the spleen, and likewise that the melanotic infiltration was *intracapillary*. Whether in similar cases the transportation of cells takes place through other channels—perhaps by means of the hepatic artery—must be left undecided for the present.

In Block's previously mentioned case of primary pigment cancer of the liver, the new-formation presented a pronounced alveolar structure, and the cells lay immediately in contact with each other; that is to say, there was no inter-cellular substance. Block regards the alveoli as dilated capillaries, between which the hepatic cells gradually and completely disappear, and considers the pigmented cells which form the contents of the alveoli as the offspring of the endothelium of the vessels, or of the cells of the capillary walls. He likewise succeeded in discovering, in the connective-tissue stroma of the endothelioma, capillaries which were in process of formation, and were connected with branches of the hepatic artery.

Sometimes the nodular pigment cancer of the liver presents the peculiar appearance of *radiated sarcoma;*[1] that is to say, rather thick white fibrous cords, which radiate through the black nodes and divide them into acini or lobules. According to Rindfleisch,[2] this peculiar structure is explained by the fact that "the capillaries, as far as to the point where they empty into the hepatic veins, are plugged by black cancer-cells, in consequence of which the familiar spindle formation by which this

[1] See *Frerich's* plate, Atlas zu den Leberkrank. 2. Heft. Taf. IX., Fig. 3. Virchow's krankhaf. Geschwülste. II., S. 286.

[2] See his Pathol. Gewebelehre. 5. Auflage. S. 431.

part of the vascular apparatus is distinguished occurs in th forms of stars of every possible dimension." According to thi the pigmented radiated cancer of the liver may be directly classed with infiltrated pigment cancer, and their histogenesi is similar.

4. *Adenoma of the Liver* (*Adenoid Liver*).

This form of tumor, partly because of its still disputed rela tionship to carcinoma of the liver, has excited a most lively interest among histologists; at the same time, there have been but few opportunities for the clinical study of the disease. For the number of cases of adenoma of the liver which have been hitherto observed and described is very small, and, moreover, as Hoffmann[1] has already stated in detail, it is undoubted that tumors of very dissimilar dignity and extraction have been designated by this name. In many of the cases the tumors which have been described as adenoma of the liver could not in any possible way be said to have any relation to cancer. In others, on the contrary, the liver was studded with tumors, which, without the aid of the microscope, would certainly have been classed with carcinoma, especially since their symptoms and course would soonest suggest a cancerous degeneration of that organ, although they present certain deviations from the ordinary clinical history of carcinoma of the liver. The number of the latter cases, which alone concern us here, as already remarked, is very limited. I include under this head Griesinger's case,[2] which furnished Rindfleisch[3] with the basis of his excellent exposition of the histology of adenoid liver, Greenfield's[4] case, that observed by Kelsch and Kiener,[5] and a briefly described case by Birch-Hirschfeld.[6]

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[1] Virch. Archiv. XXXIX., S. 203.

[2] Arch. d. Heilk. V. 1864. S. 385, with plates.

[3] Idem. See also his Pathol. Gewebelehre. 5. Aufl. S. 427 et seq.

[4] Transact. of the Path. Soc. (of London). XXV. 1874. S. 166.

[5] Arch. de Physiol. norm. et pathol. No. 3. 1876. Abstract in Virchow-Hirsch's Jahresber. 1876. I., 2, S. 285. The original has fine microscopic plates.

[6] Lehrbuch d. pathol. Anat. S. 958.

In all the cases cited the tumors in question were not single, but multiple. The liver, greatly enlarged, contained many hundreds of nodules, from the size of a poppy-seed, and less, to that of a pea, or even larger. Besides these, there are commonly several larger nodes, of about the size of a hen's egg. The nodules are strewn throughout the whole liver, and appear prominently upon the surface of the organ in the shape of rounded protuberances. Seen upon a cut section, the larger nodules exhibited a capsule of delicate connective tissue; the smaller ones, on the contrary, although distinctly circumscribed, were in immediate contact with the hepatic substance. The tumors either presented a homogeneous aspect, or showed by their lobular design that they originated in a confluence of smaller nodules. Adenomata are somewhat softer and more succulent than the liver tissue, and their cut surface projects a little above the latter. They present a great variety of coloration. In general it varies between whitish gray and pale yellow. When very vascular, they assume a reddish, even a bright red, aspect. Frequently they show a lively yellow, yellowish, or olive green tone of color, which depends upon the varying amount of biliary matter they contain. On pressure the adenoid nodes discharge only a scanty quantity of rather clear, sero-mucous fluid, but neither cancer-juice nor creamy fluid. After a time the larger nodes undergo retrogressive changes, especially a widespread and high degree of fatty degeneration of the tumor-cells; hemorrhages, more or less profuse, also occur in the softened tissue, by means of which the original condition of the tumors is so changed that they become unrecognizable. As a general thing, the hepatic tissue between the adenoid nodules retains its original characteristics; if larger nodes be present, a stasis of bile may occur, giving the adenoid nodules, as well as the liver tissue, an icteric color.

So far as we may judge from the limited observations at our command, adenoma of the liver, even when largely developed in its original location, as a rule retains the character of a local disease. It confines itself to the liver, extending neither to its lymphatic glands nor to distant organs. In Greenfield's case, however, in addition to the formation in the liver (regarded as primary), adenoid nodes existed in the lungs and mediastinal glands.

In its intimate structure, adenoma of the liver differs from cancer much more decidedly than in its macroscopic characteristics. As its name indicates, adenoma is constructed after the type of genuine glands, especially the tubular variety. Its glandular tubules in part lie parallel with each other, and partly interlaced in a sort of net-work, being connected with the inter-acinous biliary-ducts in the same manner as the rows of hepatic cells. The adenoma tubules, especially upon a transverse section, possess a marked similarity to the convoluted tubes of the cortex of the kidney. The single layer of their epithelium consists of cells varying in shape from short cylindrical to cubic. Within the lumen, which is surrounded by epithelium, lies a tough, mucoid homogeneous mass of yellowish or greenish color, which has been considered an analogue of glandular secretion. The glandular tubules are sustained and held together by a connective-tissue stroma, which likewise serves as a support for the blood-vessels. A close net-work of capillaries enwraps the tubules—the source of their supply, at least in the smaller nodes, being the branches of the portal vein.

In relation to the origin and growth of adenoma of the liver, it has been discovered, by the aid of the microscope, that the tubuli proceed from the rows of hepatic cells and the glandular cells spring from the hepatic cells themselves. In a given region the cells of the liver at first undergo an enlargement, and these hyperplastic cells immediately increase by fission. The cells which have thus originated, now arrange themselves in a circular order about a central biliary capillary, and thus create a cellular tube or glandular tubule. During this transformation of the trabeculæ of hepatic cells into adenoma tubules, the capillaries at first remain unchanged. The subsequent growth of the nodes proceeds in a variety of ways, partly by the transference of the hyperplasia and change of type to neighboring hepatic cells, partly through confluence of the nodules, and, finally, by means of a formation of lateral off-shoots from the already existing cellular tubules. In certain cases adenoma of the liver perhaps owes its origin not to the process just described, but rather to a hyperplasia of the epithelium of the biliary-ducts, in conjunction with which lateral branches push out from the finer, inter-acinous

bile-ducts, and subsequently develop into long tubules which push the hepatic tissue[1] before them.

It would be an interesting question—not alone from a histological point of view—to determine the relationship existing between the adenomas and certain other closely allied new-formations of the liver on the one hand, and primary hepatic cancer on the other hand. Our own studies in this direction have led us to believe that a gradual transition occurs in spots from partial hyperplasia of the hepatic cells (which is especially observed as vicarious hyperplasia after the atrophy of the parenchyma of the liver) to the so-called *multiple, nodular*, hyperplasia of the hepatic tissue (*Friedreich*), and thence to the genuine adenoma of the liver. These conditions are, therefore, identical in their essence, and deviate from each other only in subordinate and extrinsic points. I am, further, of the opinion that a gradual transition likewise occurs from adenoma to true primary cancer of the liver, and that under certain circumstances—*e. g.*, when it becomes irritated or in some way excited to a more rapid growth—the former may be transformed into the latter, and that the typical new-formation of glandular epithelial cells and glandular tubuli may change to an atypic and cancerous growth. Adenoma is, as it were, a histological stepping-stone for primary cancer. The new-formation may remain in this condition permanently, or for a longer or shorter period, but it may also lapse, sooner or later, into carcinoma. This view rests chiefly upon the fact that during the development of primary cancer, every one of the processes to which attention has been called can be observed side by side: thus hyperplasia and proliferation of the hepatic cells, widening of the trabeculæ of liver cells, or their transformation into glandular tubuli with a wreath-shaped arrangement of the epithelium (adenoma); finally atypic proliferation of cells and degeneration of pre-existing glandular tubules into cancer-ducts and cancerous alveoli.

5. *Sarcoma and Related Forms from the Series of Connective Substances (with the exception of Melano-Sarcoma).*

A series of morbid growths, which, from our modern, histological point of view, must be designated as *sarcoma*, occur in the liver under conditions which cause them to simulate genuine carcinoma to such an extent that we are unable to differentiate them without the use of the microscope. Sarcomatous tumors of the liver have been regarded, almost without exception, as carcinoma. This was so not only at earlier periods, but even to-day, when the terms cancer and sarcoma are more sharply defined, it still frequently occurs. Indeed, it is undoubtedly true that even a

[1] See *Birch-Hirschfeld*, loc. cit.

physician, who is perfectly familiar with the pathological anatomy of morbid growths, is not able, under all circumstances, at least during life, to recognize sarcoma of the liver, as such, or differentiate it from genuine carcinoma. This, however, is justified by the fact that, at present, we still classify the sarcomas and kindred tumors of the liver under the category of hepatic carcinoma.

Sarcoma of the liver is by no means so rare as has been commonly supposed until recently. As a *primary* growth, sarcoma, indeed, has been found in the liver in but few instances. On the contrary, the sarcomatous metastases develop in the liver with a certain degree of preference (still more frequently, however, in the lungs, serous membranes, and in the kidney and pancreas); and it is precisely these *secondary* hepatic sarcomas which present the greatest similarity to ordinary cancer.

In the majority of cases of metastatic sarcoma of this organ, the morbid growths attain so small a volume, or exist in such limited number, that, *intra vitam*, they are quite overlooked, especially when they are imbedded in the hepatic parenchyma. They are then only discovered accidentally on autopsy. In individual instances, however, secondary hepatic sarcomata reach such a development, or appear in such number, that the liver acquires a colossal volume, and a weight of three to five times its normal figure, possessing, accordingly, great resemblance to an ordinary cancerous liver. We then find the liver more or less uniformly studded with dozens, even hundreds, of nodes, which usually are sharply defined against the compressed hepatic substance, and appear as rounded elevations on the surface of the organ. The serosa upon these knobs is cloudy; distinct umbilication, however, is lacking. More rarely the sarcomatous formation in the liver occurs either as a diffuse infiltration, with a more or less complete supplantation of the hepatic parenchyma, or in the form of nodes, whose borders lose themselves in the surrounding tissue, like an infiltration. The latter condition may especially be observed in medullary lympho-sarcoma.

The remaining characteristics of hepatic sarcoma change according to the peculiarities of the primary tumor. *Fibro-sarcomas* possess a firm, brawny consistence and a whitish tint.

Their cut surface is homogeneous or indistinctly striped. Under pressure they give issue to a scanty liquid, of a clear, slightly mucoid character.[1] The same may be said of *myo-sarcoma*, which is extremely rare as a secondary tumor of the liver.[2] Secondary *osteo-sarcoma* (malignant osteoid of Joh. Mueller) appears in the liver, not of hard, bony consistence, like the primary tumor, but in the shape of distinctly circumscribed nodes, of a soft, medullary aspect. Secondary *lympho-sarcoma* of the liver occurs the most frequently, especially as the soft, medullary variety, very rich in cells, and exhibiting great similarity to medullary sarcoma. I have also observed in the liver so-called hard lympho-sarcoma. Medullary lympho-sarcomata,[3] both in the form of nodes and of infiltration, are also especially distinguished by the fact that, when the cut surface is pressed upon by the knife-blade, it discharges a thick, creamy juice, thus rendering it still more similar to cancer.

When we consider the nature and location of the primary tumor, it will not be difficult, as a rule, to diagnosticate sarcoma of the liver, as such, or to differentiate it from cancers of an epithelial nature. In the rarer cases in which the source of the morbid growth cannot be ascertained with certainty, the diagnosis of sarcoma must be effected by the microscope. The histology and genesis of hepatic sarcoma have not hitherto been thoroughly investigated. In all probability they proceed from cell-germs which have wandered into the liver. In the presence of the growing mass of the sarcoma, the parenchyma of the liver remains perfectly passive, and becomes compressed. The development of sarcomatous metastases in the liver is usually quite rapid; for this reason retrogressive changes do not readily occur.

Other tumors which belong to the series of the connective substances, such as fibroma, chondroma, glioma,[4] etc., occasionally make their appearance in the liver;

[1] I saw the liver of a lad, eighteen years of age, studded with at least one hundred dense tumors of tendinous aspect, and on the average as large as a hen's egg, between which only small strips of the atrophied hepatic tissue remained. The liver was enormously enlarged, weighing nearly fifteen pounds. The primary fibro-sarcoma apparently originated in the tendon of the biceps femoris.

[2] The only case known to me is described by *Brodowsky* in Virch. Arch., 67. Bd., S. 227. The primary myo-sarcoma was located in the stomach.

[3] See the very instructive case of *Wagner's* in the Arch. d. Heilk., VI., 1865, S. 53. The point of origin of the new-formation is not distinctly noted.

[4] The case examined by *Bizzozero* (Moleschott's Untersuchungen, X., 1869), of secondary glioma of the liver, is of especial interest, because, like the diffuse melano-sarcoma of the liver just described, it owed its origin to a growth of intra-capillary cells.

but, aside from their extreme rarity, they do not readily lead to a mistake for carcinoma. Since they are commonly isolated, reach but a moderate volume, and have a relatively prolonged development, they are, for the most part, first noticed in the cadaver, where the recognition of their histological nature cannot be difficult.

CLINICAL ASPECTS

OF

CANCER OF THE LIVER.

LEICHTENSTERN.

CLINICAL ASPECTS OF CANCER OF THE LIVER.

Bayle, Diction. des scienc. méd. T. III., Art. Cancer. Par., 1812.—*Andral*, Clin. méd. 1829–1833. T. IV., p. 188.—*Derselbe*, Préc. d'anat. pathol. Par., 1829. T. II., p. 604.—*Hope*, Principl. and Illustrat. Fig. 90–109. Lond., 1834.—*Carswell*, Illustrat. of the Element. Form of Diseases. Lond., 1838. Fasc. II., Pl. 4. Fasc. IV., Pl. 1.—*Cruveilhier*, Anat. pathol. Par., 1835-1842. Livr. 12, Pl. 2, 3; L. 22, Pl. 1; L. 23, Pl. 5; L. 37, Pl. 4.—*Th. Meyer*, Unters. üb. d. Carc. der Leber. Basel, 1843.—*J. Abercrombie*, Kankh. d. Magens, der Leber, u. s. w. Uebers. v. Gerh. v. d. Busch. Bremen, 1830. S. 444 ff.—*Halla*, Ueb. Krebsablag. in inneren Organen. Prag. Vierteljahrschr. 1844. 1.—*Oppolzer*, Ueb. d. Medull. Sarkom d. Leb. Ibid., 1845. 2.—*Bochdalek*, Ueb. d. gl. Gegenst. Ibid., 1845. 2.—*Dittrich*, Ibid. 1846. 2. 4. 1848. 3.—*Waller*, Zeitschr. d. Wien. Aerzte. 1846, Sept., Oct.—*Lebert*, Traité prat. des malad. cancer. Par., 1851.—*Koehler*, Die Krebs- u. Scheinkrebskrankh. Stuttg., 1853.—*Budd*, Diseas. of the Liver. Lond., 1854.—*Bamberger*, Krankh. d. chylopoët. Apparat. in Virchow's Handb. d. spec. Path. u. Therap. VI. 1, S. 599.—*Meyer*, Zeitschr. f. rat. Med. N. F. III., S. 136.—*A. Hirsch*, Handb. d. hist. geogr. Path. Erl., 1862–1864. 2. Bd., S. 321.—*Luschka*, Arch. f. path. Anat. v. Virch. Bd. IV., S. 400.—*J. Wilks*, Transact. of the Path. Society. Vol. X.—*Boettcher*, Arch. f. path. Anat. Bd. XV., S. 352.—*van der Byl*, Transact. of the Path. Soc. Vol. IX., p. 207.—*Rokitansky*, Lehrb. d. path. Anat. Wien, 1861. III. Bd., S. 260 ff.—*Virchow*, Verhandl. d. Würzb. Gesellsch. I. Bd., u. Ges. Abhandl., S. 155.—*Frerichs*, Klin. d. Leberkrankh. 1861. Bd. II., S. 271 ff.—*E. Wagner*, Die Struct. d. Leberkrebs. Arch. d. Heilk. 1861. II., S. 209.—*E. Rollet*, Wien. med. Wochenschr. 1865. XV. 14, 15.—*Naunyn*, Reichert's u. Du Bois-Reymond's Arch. 1866. H. 6.—*Murchison*, Clin. Lect. on Diseas. of the Liv. Lond., 1868, S. 187 ff.—*Schueppel*, Arch. d. Heilk. 1868, S. 387.—*Fetzer*, Beitr. z. Histogenese d. Leberkrebs. Disser.-Inaug. Tübingen, 1868 (præside Schueppel).—*Wulff*, Der prim. Leberkr. Dissert.-Inaug. Tüb., 1876 (præs. Schueppel).—*Riesenfeld*, Dissert.-Inaug. Berl., 1868.—*E. Hess*, Zur Path. d. Lebercarc. Diss.-Inaug. Zürich, 1872 (Klinik v. Biermer).

Historical Sketch.

It was not until the Renaissance of anatomy, in the sixteenth and seventeenth centuries, that the various anatomical changes in the liver—enlargement (obstructiones), condensation (indurationes), abscesses and softening (apostemata, colliquationes), tumors, cysts, "steatoma," tubercles, scirrhus, infarctions—gradually became known.[1]

In the great anatomical compilations of the seventeenth century, and in the later works of Lieutaud, Sandifort, and Baillie, are descriptions of hepatic tumors which undoubtedly were either carcinomata, or other malignant neoplasms. It was held that all these tumors, as Galen had taught, were the result of inflammation of the liver, or the consequence of metastasis of the tumors, which later gave rise to the term "congestion" or infarctus of the liver.

The interpretation of hepatic cancer as an especial anatomical form of disease, and its differentiation from other kinds of induration and tumor formation, belong to the close of the last century, and particularly to our own.

Bayle's[2] excellent researches laid the foundation for the anatomical discrimination between cancer and tubercle. The anatomo-pathological bent which was imparted to medicine by

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[1] Induration, scirrhus, and tumors of the liver were also described, by the physicians of antiquity, as the sequelæ of inflammation of this organ. Anatomical demonstrations of the nature, appearance, and peculiarities of these growths and indurations were not given. (*Hippokrates*, Aphorism., Sect. VI., Edit. Kuehn, III., S. 755.—*Galen*, Method. Medendi., Lib. II., C. VII.—*Aretæus*, De caus. et sign. acut. morb., L. I., C. XIII. Ed. eadem, S. 109.—Several excellent descriptions by *Morgagni*, Ep. 30, Art. 14, Ep. 38, Art. 28. Also Art. 30, 31, a fine description of granular liver. See also Ep. 36, Art. 25.)—The medical authorities of that day accepted the anatomical discoveries, but held to their opinion, that the various tumors, tubercles, and steatoma were due to inflammation. (*Bianchi*, Hist. hep., Lib. I., p. 336.—*Fr. Hoffmann*, Diss. méd. de hep. Scirrho., 1722.—*van Swieten*, Comm. in H. Boerhave Aphor., Lib. III., p. 117.—*Stoll*, Rat. med., Tom. III., p. 1.—*M. Baillie*, Anat. d. krankh. Baues. Uebers. v. Soemmering, Berl., 1794, S. 130.—*Portal*, Malad. du foie, Paris, 1813.—Cit. by *Frerichs*, l. c., S. 271.)—Several valuable historical communications in the Ephemerid. medico-phys. German. Acad. Cæsareo-Leopold. nat. curios., 1670, anni sq. See the historical notices by *R. Koehler*, Die Krebs- und Scheinkrebskrankh. Stuttg., 1853, S. 360.

[2] Diction. des Scienc. méd. Paris, 1812. Art. Cancer.

the works of Bichat, Bayle, and Laënnec, and which secured firmer foothold as our century advanced—particularly the rapid progress in microscopical research, and finally the application of the cellular theory to pathological processes—have united in illuminating every portion of the hitherto darkened field of pathological neoplasms. Nor has reform in special clinical departments been wanting. The mistaken and unintelligible conceptions of "congestion of the liver," infarctus, and obstruction also gradually fell into discredit from a clinical point of view. The need of an anatomical differential diagnosis became imperative, and finally conquered the field of medical thought which previously had been occupied by venerated but false theories.

How powerfully this reform in the clinical department of medicine was supported and advanced by the contemporaneous discovery of the method of examination by physical diagnosis, hardly requires mention.

Etiology.

However much the *anatomical* nature of cancer may have been explained through the achievements of pathological anatomy, the question concerning the *etiology* of this disease has suffered the fate of most etiological questions—it has remained unanswered. But even in this particular a progress is to be noted, which should not be undervalued, although it is directed merely to the negative aspect of the question. The divers etiological theories which existed in the earlier periods of our century, at the time of the philosophico-natural school — theories universally accepted and held as true, but which culminated in mere fantastic vagaries and empty phrases—have deservedly lost credence, and the conviction has been reached that in the present condition of our positive knowledge the *etiological nature* of cancer cannot be discovered.

Certain causative factors which hold an intimate relation to the etiology of hepatic cancer have become known to us; if our statistics were more serviceable, the influence of these factors might be shown with greater certainty by the use of reliable figures. Let us examine the more important of these points.

1. *Heredity.*—In his epochal work upon diseases of the liver, Frerichs remarks that "the data heretofore established are not sufficient to secure to heredity a positive influence." But there are many facts, not proved indeed by statistics, which are nevertheless assured. Among them belongs the *heredity* of cancer. Its influence has long been generally acknowledged, and I believe with reason. That which applies to cancer, in general, self-evidently and as a matter of experience, equally applies to cancer of individual organs.[1]

Without sparing labor, I have examined the well-arranged archives of the Tübingen Medical Clinic, for many years, upon the point in question. The results are meagre. In sixty-eight cases of *various sorts of cancer of internal organs*, heredity was mentioned in eight (12%); in the remainder its absence was equally positive. The most extended statistics of *heredity* of cancer in general with which I am familiar are those I have collected, viz.:

Paget[2]	333	cases,	of which	83	were hereditary.
Cooke	79	"		21	" "
Sibley[3]	305	"		34	" "
Lebert	102	"		14	" "
Lafond[4]	71	"		7	" "
Hess	25	"		1	was "
Tuebing. Med. Clin	68	"		8	were "
Moore	144	"		24	" "
Total	1127			192	

Seventeen per cent., therefore, were hereditary.

The hereditary element also plays a subordinate part in cancer of the liver. For obvious reasons we are unable to present and compare statistics of its influence. Statistics which, as in the foregoing cases, *must* be based upon the statements of patients, are always extremely doubtful. We can only rely upon the

[1] I may refer to various papers, which, while not free from objections, are nevertheless important and interesting essays: *C. H. Moore*, "A Brief Report on Cases of Cancer," Brit. Med. Jour., 1866, Dec. 1, 1866; *Morant Baker*, "The Inheritance of Cancer," etc., St. Barthol. Hospital Reports, II., 1866, p. 129, and Brit. Med. Jour., 1867, April 27, p. 476; *Cooke*, Th. Weeden, "On Cancer," London, 1865.

[2] Cited by *Cooke*, *M. Baker*, et al.

[3] Middlesex Hosp., 1853–1856. Med.-Chir. Transact., 1859, XLII., p. 111.

[4] Cited by *Hess*, l. c. This author has read *Moore's* and *Morant Baker's* figures incorrectly.

clinical histories of the material of the larger clinics; these would be useful if the history were obtained with equal care in all cases, and the results registered even when negative.

In 12 cases of cancer of the liver in the Tübingen Clinic, I found that heredity was "clearly proven" in two. E. Hess reports 25 cases in the Clinic at Zurich, among which heredity was proven in only one.

2. *Age.*—The old-established fact, known long before the introduction of statistics, that cancer is more common at a more advanced period of life, especially in persons over forty years of age, than in youth, naturally applies with equal force to cancer of the liver.

472 cases of cancer of the liver, collected by myself, showed the following results in this regard:

	Age in Years.					Total.
	20–30	30–40	40–60	60–70	O'er 70	
1. Koehler, loc. cit., S. 378	8	8	33	16	7	72
2. Geneva Clinic, 1838 to 1855	3	8	51	19	12	93
3. Frerichs, loc. cit., S. 294	7	14	41	19	2	83
4. Smoler,[1] Prague Clinic	2	6	37	7	2	54
5. Riesenfeld, Path. Inst., Berlin, 1864 to 1868	5	14	30	16	4	69
6. E. Hess, loc. cit., S. 10 (Biermer's Clinic)	11	9	50	13	6	89
7. Tübingen Med. Clinic, 1871 to 1876	1	2	8	1	....	12
Total	37	61	250	91	33	472
Per cent	7.8	12.9	53.1	19.3	6.9	

Like carcinoma in general, cancer of the liver in children is extremely rare. Siebold[2] observed cancer of the liver in a newly born child; Farre[3] saw a secondary hepatic carcinoma in a child three months old, and two cases at two and one-half years of age. Cornil[4] describes an hepatic myxoma occurring in a girl eight months old; Kottmann,[5] a case of primary hepatic cancer in a child of nine years; Roberts,[6] another in a girl of twelve; I have myself seen cancer of the peritoneum and liver in a boy of seven.

[1] Cited by *E. Hess*, loc. cit., S. 10.
[2] Canstatt's Jahresber. 1854. IV., S. 319.
[3] Cited from *Frerichs*, loc. cit. S. 293.
[4] Gaz. méd. de Paris. 1872.
[5] Correspondenzbl. d. Schweiz. Aerzte. 1872. No. 21.
[6] Lancet. I., 3. Jan., 1867. Schmidt's Jahrb. Bd. 135, S. 25.

3. *Sex.*—Statistics have long shown that cancer in general affects the female sex oftener than the male.[1] The reason for this lies in the extraordinary frequency of mammary, uterine, and ovarian carcinoma.[2] If these forms of cancer be excluded from any extensive statistics (*e. g.*, those of the Geneva Clinic), the frequency will be found to be so nearly the same in the two sexes that a preponderance on the side of the female sex can hardly be said to exist.[3]

Since cancer of the liver, in the great majority of cases, is *secondary*, following not only cancer of the stomach, but also carcinoma of the ovaries, uterus, and mammæ, it becomes evident that females are oftener attacked than males.

This is shown by the following statistics which I have compiled, but which apparently do not distinguish between primary and secondary cancer of the liver. The authors in question give no definite statement, at least on this point.

	Males.	Females.	Total.
Oppolzer[4]	9	21	30
Halla[5]	6	1	7
Lebert[6]	6	8	14
Heyfelder[7]	24	15	39
Wilkinson[8]	9	21	30
Ulrich[9]	5	6	11
Van der Byl[10]	13	16	29
Frerichs[11]	10	21	31
Hess[12]	18	17	35
Biermer[13]	18	10	28
Riesenfeld[14]	32	37	69
Prague Pathol. Institute[15]	96	132	228
Vienna General Hospital[16]	88	117	205
	334	422	756

[1] Adding the figures of the London Clinics (1849–1859) to those of the Geneva Clinic (1838–1855), we obtain a proportion of 12,019 deaths from cancer in males to 29,308 in females; or, 1 : 2.44.

[2] Twenty-five per cent. of all cancers are mammary, uterine, and ovarian. (Geneva Clinic, 1838–1855.)

[3] Compare *Oesterlen*, Med. Stat. Tübingen, 1865. S. 432.

[4] Prag. Vierteljahrschr. 1845. II., S. 65. [5] Ibid. 1844. I. [6] Op. cit., S. 537. [7] Stud. im Geb. d. Heilk. I. Th. Stuttg., 1838. [8] and [9] Cit. by *Hess*. [10] and [11] Loc. cit. [12] and [13] Cited by *Hess*, loc. cit., S. 12. [14] Loc. cit. [15] Jahrg. 1850–1855, und 1856. Cited by *Hess*. [16] Jahrg. 1858–1874 (with exception of 1871). Compiled by myself from the records of the Imperial Vienna Hospital.

Besides the etiological factors already named, others are often mentioned, especially wounds in the vicinity of the liver.[1] Frerichs considers it probable "that under favoring conditions external injuries may be the *first step* in the altered nutrition of the hepatic substance." A previous contusion or blow, as well as a "cold," very frequently satisfies the desire of the patient to refer the disease to some cause, when etiological factors are entirely unknown. The abuse of alcohol is also arraigned, but with even less reason, for the female sex perhaps is more frequently subject to cancer of the liver than the male. The assertion that depressing influences, trouble, and care, insufficient nourishment, or (as others assert, on the other hand) a luxurious, indolent life (Budd)—"plethora"—and obesity predispose to cancer of the liver, is made out of whole cloth. Supported by the well-known fact that cicatrices, warts, and nævi are sometimes the place of origin of cancer, certain writers have affirmed that carcinoma occasionally finds its origin in pathological aggregations of connective tissue in the liver, or in the neighborhood of the portal vein and the larger bile-ducts. Cases are here included in which hepatic cancer occurred in a cirrhotic (granular) liver. Recklinghausen[2] has seen an exquisite example, and I have observed another. Cases are also mentioned in which, following a severe attack of gall-stone colic, the cancer of the liver "probably" originated in collections of connective tissue in the neighborhood of the gall-ducts, due to the irritation caused by the calculus.[3] Whether this interpretation of these cases be correct or not, we may at least affirm that their occurrence is so extremely rare as to have little or no etiological value. (See Schueppel's remarks on this point in the section on Path. Anatomy.)

Geographical Distribution.—Cancer of the liver occurs in every climate. Somewhat frequent in the temperate zones, it *appears* to be rarer in the tropics and sub-tropics. According to the united testimony of credible and experienced writers, this disease is very rarely encountered in India. "I have never seen a

[1] *Leared*, Trans. of the Path. Soc. 1869. XIX.

[2] *Rosenblatt*, Diss.-Inaug. Würzb., 1867.

[3] *Williglc*, Virch. Archiv. Bd. 48, S. 524.

single instance of cancerous deposition in the liver in this country," says Webb, who, in this particular point, is a very competent judge, "not even in cases where the disease has been well manifested in the uterus, stomach, and intestines;" and Morehead[1] expresses himself in similar terms.

In the majority of cases, cancer of the liver is secondary.

It is at once apparent that statistics concerning the relative frequency of *primary* and *secondary* cancer possess a subordinate, at most only an approximative value. I present the following statistics with every reservation:

Sibley, loc. cit.....	63 cases.	3 primary.	60 secondary.
Van der Byl, loc. cit.....	29 "	3 "	26 "
Riesenfeld, " "	69 "	10 "	59 "
Frerichs, " "	31 "	10 "	21 "
Oppolzer, " "	53 "	17 "	36 "
Pemberton,[2] " "	51 "	18 "	33 "
Meissner,[3] " "	109 "	5 "	104 "
Biermer,[4] " "	25 "	6 "	19 "
Total.....	430 cases.	72 primary.	358 secondary.

The relative frequency of primary to secondary cancer is therefore 1 to 5.

If we ask, "In which organs does cancer most frequently give rise to secondary cancer of the liver?" the answer would simply be: 1. Those organs which empty their blood into the portal vein—namely, the stomach, the intestines (especially the rectum[5]), the peritoneum, and the pancreas. Cancer of the uterus and of the ovaries, as we are taught by abundant examples, is likewise not unfrequently followed by secondary hepatic cancer. It is to be remembered that the veins of the peritoneal investment of the internal genital organs communicate with the branches of the portal vein, and, also, that constant anastomoses exist between the venæ uterinæ and the venæ mesentericæ. 2. Secondary cancer of the liver naturally follows that cancer most frequently which occurs oftenest. Cancer of the stomach holds the

[1] Quoted from *Hirsch*, Hist. Geogr. Path. II. Bd., S. 321.

[2] Quoted from *Hess*, l. c., S. 14.

[3] Ibidem. [4] Ibidem.

[5] Constant anastomoses between the vena hemorrhoidalis inferior of the plexus hemorrhoidalis and the v. hemorrhoidalis superior of the vena mesenterica inferior.

first place, and is followed in frequency of occurrence by cancer of the uterus, mammæ, rectum, peritoneum, pancreas, and lymphatic glands. (See Schueppel on Pathological Anatomy.)

Secondary cancer of the liver may follow cancer of the most dissimilar organs, and in very widespread carcinoma the liver is uniformly involved.

On the other hand, hepatic carcinoma will itself give rise to the secondary form of cancer. Especial mention may be made of pulmonary and pleural carcinoma (metastasis through the blood-vessels); and, further, of cancerous degeneration of the lymphatic glands (the hepatic glands in the portal fissure and the cœliac glands). The *deep* lymphatics of the liver pass through these glands, and the superficial lymphatics pass into the suspensory ligament, reach the diaphragm, and then run behind the xiphoid cartilage, and anastomose with the anterior mediastinal and mammary plexuses of lymphatics. Since still other lymphatics pass from the liver to the glands of the *posterior* mediastinum, it is easily seen that in hepatic cancer a secondary development may follow varied and very divergent paths. It is not my office to pursue all these paths, especially so because the most important facts concerning the dissemination of hepatic cancer through the veins, the lymphatics, and the biliary ducts have already been set forth in the chapter on the pathological anatomy of the subject.

With regard to the *frequency of cancer of the liver* in the scale of comparison with cancer in general, we may sufficiently answer the question—which at present has only a statistical interest—by means of the computation which follows:

I take these figures from the records of the Imperial Hospital of Vienna:

From the year 1858 to 1874 (not including 1871) 368,548 patients were treated; of these 205 suffered from carcinoma of the liver. Among 1,798 patients, suffering from the greatest variety of *internal* and *external* diseases, there was, therefore, *one* case of cancer of the liver.[1] Taking *internal* diseases alone, the proportion, of course, is notably different, viz., 1 : 322.

The universally accepted statistics of Oppolzer, who found 53 cases of cancer of the liver among 4,000 (!) diverse internal diseases, or 1 : 76, hardly require a refutation. Still more useless are the many smaller statistics, which, almost without exception, give far too large a proportion of cases of hepatic cancer as compared with other affections.

The post-mortem records[2] show that in 6,019 *bodies of patients, who died from various diseases*, 174 exhibited cancer of the liver. Proportion, 1 : 34.

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[1] These statistics likewise clearly show the greater relative frequency of hepatic cancer in women. Among 232,840 male patients there were 88 cases of cancer of the liver (1 : 2,646); of 135,708 female patients 117 had hepatic carcinoma (1 : 1,160).

[2] *Van der Byl*, l. c. *Foerster*, Prager pathol. anat. Inst. 1850–55 and 1866. Cited by *Hess*, l. c., S. 13.

What place in the scale of frequency does cancer of the liver hold in relation to cancer in general?

Tanchou's statistics of cancer, obtained from the civil records of the departments of the Seine, are notably defective. Among 9,118 fatal cases of cancer, there were 578 cases of cancer of the liver; the proportion is therefore 1 : 16.

The records of the Imperial Hospital of Vienna show that of 368,548 patients, 5,955 suffered from carcinoma (*i. e.*, malignant neoplasms) of *various* organs; and of these there were 205 cases of cancer of the liver; that is to say, in 29 cases of cancer, one case was hepatic carcinoma.

Finally, the Geneva statistics (1838–1855) give 93 cases of cancer of the liver in 889 fatal cases of general carcinoma. Proportion, 1 : 9.5.

Combining these three records, we have 15,962 cases of cancer of all organs, of which 876 were cancer of the liver. Proportion, 1 : 18.

Cancer of the liver, perhaps, occupies the fourth place in the scale of relative frequency of carcinoma in all organs. It is preceded by cancer of the uterus, stomach, and mammary glands.

Calculating from the tables of Tanchou and Marc d'Espine, the total being 10,007 deaths from cancer, we have the following percentage of frequency:

Cancer of the	uterus	31 per cent.
" "	stomach	27 "
" "	mammæ	12 "
" "	liver	6 "
"	of all other organs taken together	23 "

Symptoms and Diagnosis.

The morbid picture created by cancer of the liver in many cases is so pregnantly characterized by the presence of numerous symptoms on the part of the affected organ, that a diagnosis is exceedingly simple. In other cases this is difficult, and can only be done with a certain degree of probability, or is even impossible; these are cases in which all those symptoms are lacking which would justify us in supposing the existence of disease of the *liver*.

Let us first consider the cases in which cancer of the liver pursues a *latent* course. In the first place are to be mentioned those not infrequent cases in which we have positively diagnosticated carcinoma of the stomach, rectum, peritoneum, uterus, the mammæ, etc., and in which the diagnosis is confirmed by the autopsy; at the same time numerous secondary cancerous nodes

likewise exist in the liver, which during life were indicated by no symptoms whatever. In many of them diagnosis might have been made possible by changes in the shape and external surface of the liver, had not the meteorism of intestinal cancer, or the ascites of cancer of the peritoneum, or gastric dilatation of carcinoma of the pylorus, forced the liver upward from the anterior wall of the abdomen, and so made palpation impossible. *Secondary cancer of the liver, in very numerous instances, runs its course without symptoms, and, clinically, cannot be diagnosticated.* In many of these cases, however, the diagnosis might have been possible, perhaps, if our attention, which was wholly absorbed by the main centres of the carcinoma, had been more carefully directed to the condition of the liver, if icterus had been sought for in the conjunctivæ, or if the urine had been repeatedly examined for biliary coloring matters.

Primary cancer of the liver, likewise, pursues a latent course, sometimes for a long period. These are the examples in which an individual of ripe age at first experiences annoyances of an uncertain character: vague pains in the back and abdomen; disturbances of digestion; loss of appetite; constipation; nutrition quickly suffers; the healthy appearance gradually disappears; the color of the skin and the physiognomy become morbidly changed; the patient has a constant feeling of fatigue; he is irritable, or depressed and apathetic. At first the physician may, perhaps, consider a chronic gastro-intestinal catarrh as the cause of the disturbances in nutrition, but the daily increase of the cachexia, and the rapid loss in weight, strengthen the suspicion that a more serious cancerous affection is the origin of the disorder. Yet the most careful examination of the epigastric region and of the liver, by means of palpation and percussion, discovers nothing abnormal. Ascites and œdema of the lower extremities make their appearance, the patient becomes extremely cachectic, and dies after the disease has lasted six months or a year. The autopsy reveals numerous cancer nodes in the liver, which were either primary, or coexisted with a latent carcinoma of the stomach, of the pancreas, the retro-peritoneal glands, etc.

There are cases of cancer of the liver in which nodes soon appear upon the convex (superior) surface of the organ, and create

adhesions with the diaphragm. Very soon symptoms of a right-sided pleuritis become apparent. A right-sided exudation forms, and, as experience teaches, soon becomes purulent, and may lead to high hectic fever and profuse morning-sweats; the nutrition of the patient fails rapidly, and since icterus is not present, and the examination of the liver and epigastric region yields a perfectly negative result, a diagnosis of empyema probably will be made and considered a satisfactory explanation of the general symptoms. The autopsy shows that the pleuritis was secondary, and that it had been called forth by primary or secondary cancer nodes in the liver, perhaps coexisting with latent carcinoma of the stomach.

In still other cases cancer of the liver early gives rise to ascites, on account of the existence of growths in the larger branches of the portal vein. Inflammatory processes follow, having perhaps proceeded from cancer nodes in the portal fissure. The ascites assumes all the characteristics of a chronic peritonitis, with exudation, and the patient quickly emaciates under a hectic type of fever. The liver becomes displaced and inaccessible to palpation; icterus is not present. If such an occurrence exceptionally be met with in a young person, the diagnosis of tuberculous peritonitis, perhaps, will be made; the autopsy reveals a cancer of the liver, with chronic secondary peritonitis. A girl of fourteen, who came under my notice, was wasted to a skeleton, had a high hectic fever, and presented all the symptoms of a chronic peritonitis, with large exudation; the nodes, which were perceptible in various localities of the abdominal cavity, were supposed to be tuberculous, or simply indurated centres of inflammation, and a diagnosis of chronic tuberculous peritonitis was accordingly made. The post-mortem examination revealed a sarcomatous peritonitis, with numerous secondary nodes in the liver.

The mistakes in diagnosis, which I have just sketched, are extremely rare and exceptional. In the majority of cases the clinical history of hepatic cancer is very significant. In addition to the cancerous marasmus, there are so many symptoms on the part of the diseased organ (enlargement, with perceptible knobbed protuberances, ascites, icterus) that, if we bear in mind the age

of the patient, and the duration of the disease, the diagnosis will offer no difficulty. Let us sketch one of these unmistakable forms of disease under which cancer of the liver pursues its course:

An individual, at an advanced age, begins to complain of various difficulties of digestion; his appetite decreases, a feeling of fulness and pressure in the abdomen, painful sensations in the back, in the right hypochondrium, or in the region of the stomach, make their appearance, together with irregularity in the bowels (obstinate constipation occasionally alternating with diarrhœa). The previously healthy appearance of the patient becomes changed; the color of the face and of the entire skin becomes sallow, and changes to a dirty yellow; the features assume the peculiar, sharp, and pointed contour of the physiognomy of carcinoma. The patient rapidly loses weight, but the prominent abdomen stands in marked contrast to the skeleton-like emaciation of the rest of the trunk, of the nates and extremities. The veins of the lean, subcutaneous cellular tissue stand out like blue cords, and are made especially distinct by the dirty yellow color of the dry, parchment-like skin, which can be raised in high and long folds. The patient is always tired, and incapable of physical or mental labor. His mood is depressed, irritable, apathetic, hypochondriacal. Slight rise of temperature is temporarily observed. The periodically exacerbating and remitting pains often reach an intense degree, and extend in all directions. Icterus now appears, at times distinctly recognizable only in the conjunctiva, and at others spreading throughout the entire skin; the urine has a dark color, and yields positive results to the tests for biliary coloring matter. The examination of the liver shows that the organ is markedly enlarged, of increased consistence, and presents various irregularities and knobbed protuberances. Finally, after a duration of from six to twelve months, and after the appearance of ascites, œdema of the lower extremities, and perhaps thrombosis of the crural veins, the patient dies in the last stage of emaciation and marasmus.

There are many deviations from the combination of symptoms which I have sketched. These will be noticed in the following analysis of individual symptoms.

Condition of the Liver.—In the beginning of the disease, all objective symptoms on the part of the liver are lacking. Later it always enlarges, sometimes to a very considerable degree. The enlarging organ increases in the direction of least resistance—*i. e.*, toward the abdominal cavity. Its sharp edge projects below the borders of the ribs, in the right mammary line, for a distance equal to the breadth of four fingers or of the entire hand. In the median line, it reaches the umbilicus, or even extends somewhat below it. The border of the left lobe meets the margin of the left ribs a little beyond a prolongation of the mammary line, on a level with the ninth and tenth ribs. This is, approximately, the course of the lower border of the liver in moderate enlargement of the organ. In the majority of such cases the upper or pulmonary limit of the liver is as yet, in its normal position, at the sixth rib. On the other hand, even in this degree of enlargement of the organ, it more frequently happens that the inferior border of the lung is distinctly crowded upward for a space of two or three fingers' breadth. This condition is undoubtedly due to the greater respiratory activity of the anterior walls of the thorax as compared with that of the posterior inferior walls—a fact which finds its confirmation in the greater respiratory locomotion of the anterior inferior borders of the lung.

In many cases the enlargement of the liver becomes excessive. In extreme instances the organ attains a weight of twenty pounds (Colling, Frerichs[1]), of twenty-four pounds (Gordon[2]), and even of twenty-five pounds (Axel-Key[3]).

The liver then nearly fills the entire abdominal cavity. It extends downward to the anterior superior spine of the ileum, and in the median line to a point half-way between the umbilicus and pubes. The left lobe extends far into the left hypochondrium, lies in contact with the crenated margin of the spleen, forcing this organ downward and backward. The left complementary space in such cases often yields a dull tone and strong "percussion-resistance." The diaphragm is also forced upward.

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[1] L. c., S. 288. Remarks. [2] Dublin Quar. Journal. Nov., 1867.
[3] Hygiea. Bd. XXVII. 1865. No. 5.

The boundary-line between the liver and the lung is found at the fifth, fourth, or even on a level with the third rib, anteriorly, and at a point close under the angle of the scapula, posteriorly. Roberts, of Manchester,[1] describes a case of cancer of the liver in a girl of twelve years, in which the enormously enlarged organ (weight, ten pounds) had driven the diaphragm up to the clavicle (?), had completely compressed the lung, and even exerted pressure upon the right subclavian artery (the right pulse was perceptibly smaller than the left). The displacement of the diaphragm reaches an especially high degree, and occurs even when the liver is only moderately enlarged, if, in addition to this factor, other conditions exist—meteorism, ascites—which still further restrict the abdominal space.

The enlargement of the liver is generally in proportion to the number and size of the cancerous nodes. Sometimes it involves the whole organ ; at times it is confined to a *single* lobe, more frequently the right than the left. In certain instances the left lobe is enlarged, although only the right is the seat of cancer. Such increase of size in the left lobe, designated now and then as "sympathetic" or "vicarious" enlargement, usually originates in a parenchymatous inflammation, and in rare cases arises from a compression of the left hepatic vein, either by cancerous nodes in the lobus Spigelii, or by the growth of cancer-tissue into the vein. But the liver is not by any means enlarged in all cases of carcinoma. Very frequently in *secondary carcinoma*, if the development of the cancer nodes has occurred at a time when the *primary* cancer has already given rise to cachexia, has diminished the vascularity of the body, and has caused an atrophy of all the organs, there is no increase in the size of the liver. In such cases, though the organ may be studded with multitudinous cancer nodes, it may be even smaller than normal. The most remarkable enlargements are seen in primary cancer of the liver, and likewise in the secondary carcinomas which have found an early development in the liver, at a time when the primary growth has not yet given rise to cachexia. It appears to me also, at least according to my own experience, that the enlargement of

[1] Lancet. 1867, Jan.

a cancerous liver is, on the average, more considerable in young people than in the very old.

In the preceding pages I have already remarked that meteorism, ascites, and a marked gastric dilatation may render impossible the diagnosis of moderate hepatic enlargement.

We should be mindful of this fact when it is found that a liver, heretofore notably enlarged, after a time does not project so far downward into the abdominal cavity as formerly ; either meteorism or ascites may be the cause of this phenomenon. At the same time, cases undoubtedly occur in which, toward the close of life, an enlarged liver again becomes smaller, since the marasmus has caused a loss of parenchyma in the liver, as well as in all the other organs. This organ, of necessity, becomes smaller, unless, through the development of new elements of cancer, those portions of the normal parenchyma that have been destroyed by atrophy are replaced.

It should further be remembered that cancerous nodes in the liver may induce gradual atrophy of the normal hepatic tissue, and create an interstitial inflammation of the whole organ ; and, again, that the cancerous nodes themselves, through central cicatrization and retrogressive changes, may become smaller.

Besides the enlargement of the organ, a very important symptom of cancer of the liver is the formation of *rough, large nodular protuberances upon its surface or along its sharp border.* The latter is very easily discovered on palpation, because the consistence of the organ has become more dense. If the palpating fingers be pressed from below upward, beneath the border of the liver, and (the fingers being raised) the organ be allowed to glide downward over them, we can convince ourselves of the increased resistance of the border of the liver. Sometimes we can feel that in places the border is sharp, in others thickened, or rounded. The tumors, for the most part, are hard and resistant; this fact, however, does not prove that we are dealing with solid tumors. The tensely distended walls of a cyst, especially when palpated through the thick abdominal parietes, create the same sensation as a solid tumor. Now and then, although rarely, we can detect soft, almost fluctuating tumors. Under favorable circumstances even growths in the concavity of the liver, near the

sharp border, can be distinguished if the fingers be forced up under the latter. With regard to differential diagnosis, it is often important to determine the existence of several discrete tumors in the right lobe of the liver, as well as in the left lobe, at a distance from the former.

Occasionally the gall-bladder is secondarily affected by cancerous degeneration. In a case, which I saw in 1871, an uneven, hemispherical tumor was found projecting into the abdominal cavity, immediately over the border of the liver, and corresponding to the site of the gall-bladder. This tumor followed the respiratory movements of the liver in the most perfect manner.

Errors caused by a tight-laced fissure of the liver, by dropsy or dilatation of the gall-bladder, from obstruction of the cystic duct, by the presence of fæcal tumors in the transverse or ascending colon (which often lie immediately against the sharp edge of the liver, and sometimes exactly follow the respiratory movements of the liver, even when there are no adhesions between them and the colon), and, finally, the deceptions created by the belly of the rectus abdominis muscle protruding between two of its tendinous intersections, may be easily avoided by a certain degree of practice and careful attention.

On the other hand, it is more difficult to distinguish carcinoma of the colon, the omentum, and especially of the pyloric end of the stomach—when the tumor lies immediately upon the sharp edge of the liver—from hepatic carcinoma. Frequently the tumor is adherent to the liver; but even when this does not occur, the tumor—which can be felt and is often seen to be in apposition with the liver—is moved downward with every inspiration, and upward with every expiration. In such cases percussion is of importance only when a light blow reveals a zone of clear, intensely tympanitic notes between the liver dulness and that of the tumor. Generally, however, the decision can be made only by palpation, since percussion fails. A very careful, delicate palpation will discover that the thin edge of the liver lies over the tumor; the fingers can be inserted between the tumor and the border of the liver, and the latter may then be lifted and allowed to glide over them. In other cases we can convince ourselves that the tumor, which protrudes from just

beneath the liver, can be moved independently in a lateral direction, and, what is especially convincing, that it can likewise be moved vertically. Careful observation at different periods further shows that the tumor—for example, in carcinoma of the stomach and colon—does not always occupy the same site, but that it changes position, according to fulness or emptiness of these organs. At one time, also, it has a large volume, and is easily found; at another, it can be palpated only over a small space, or not at all. At present I will not enter upon the other points in differential diagnosis.

Sometimes a careful inspection is alone sufficient to make us certain of the existence of an enlarged liver and hepatic tumor. The right hypochondrium (including the epigastrium) is more convex; the arches of the ribs are forced outward, and the semiglobular protuberances on the surface of the liver show themselves through the thin tissues of the abdominal walls. In the right hypochondrium and in the epigastric region it will be seen that the tumors, lifting the skin, move downward with inspiration, and upward with expiration. During these movements, if the hand be laid over the tumors, a distinct friction will sometimes be felt, and not by any means so rarely as is generally believed. If the stethoscope be applied, a creaking friction sound will be heard. A strong pressure upon the tumors, or a to and fro movement of the skin over them, will also create a perceptible grating. An inflammatory roughening of the peritoneal investment of the tumors is a necessary condition in this phenomenon.

In a case of cancer of the liver, which came under my observation, a tumor was neither visible nor palpable during quiet respiration. But when the patient was directed to take a deep inspiration, a tumor emerged from beneath the bend of the ribs; its contour was easily perceived through the thin abdominal tissues, and it could be palpated without difficulty; on expiration it at once disappeared behind the costal arches.

During the course of the disease, we can sometimes prove, by a long-continued observation and by repeated and careful examinations, that the liver, or one of its lobes, is gradually enlarging and changing in shape; that tumors previously discovered are

growing in volume; that new protuberances have appeared and can be detected by palpation. In rarer cases, however, the physician may also convince himself that the liver is becoming smaller (p. 374), and that a tumor, hitherto very distinct, is less easily palpated, and perhaps has even disappeared. This may be the result of a softening of the tumor, or of contraction, or umbilication. But, so far as I know, there has been no case in which the latter condition could with any certainty be diagnosticated during life. As a general thing, the umbilication is too shallow. The enlargement of the liver usually takes place slowly, but that of the tumors may be more rapid. A hitherto barely perceptible tumor can become notably larger within eight days. Cases of this nature have been described by Budd, Andral, and Henoch. Murchison[1] was able to follow the enlargement of the liver from week to week. In one case I found it very easy to convince myself of the increase of the tumor, and in another I observed a rapid decrease in size in a previously prominent and resistant growth. A sudden and considerable enlargement of the liver, or of a tumor which has already been diagnosticated, is sometimes observed in case of hemorrhage in softened cancerous masses, or during the occurrence of a sub-capsular extravasation of blood.

Ascites and *peritonitis with effusion* are frequent sequelæ of cancer of the liver. By adding the statistics of Frerichs, Hess, Biermer's clinic, and those of general literature, I find 154 cases in which ascites and effusion were noted seventy-eight times, or 50 per cent. Murchison[2] considers the occurrence of ascites as even more common.

It usually appears during a later period of the disease, or at least at that time first attains an extent which is perceptible on percussion. But sometimes ascites occurs early; these are the very cases in which a differential diagnosis between cancer and cirrhosis of the liver may become difficult. The ascites is a consequence of a stasis in the portal circulation, which arises in various ways, sometimes through obstruction, sometimes through compression of the larger branches of the portal vein, or of its

[1] Loc. cit., p. 187. [2] Loc. cit., p. 191.

trunk. Cancerous masses in the liver extend into the larger branches of this vein, or perhaps even as far as its principal trunk, and partly obstruct it. In secondary hepatic cancer (*e.g.*, as a sequel of gastric carcinoma), this invasion of the portal vein originates in the coronary or pyloric veins of the stomach. In other cases, there is partial compression of the trunk of the portal vein by enlarged portal lymphatic glands, which have become infiltrated with cancerous matter, and have united with the portal vein in a dense conglomerated mass (periphlebitis fibrosa). A partial compression of the portal vein may perhaps be caused by great enlargement of a cancerous liver in its vertical diameter, especially if the portal lymphatic glands are simultaneously enlarged. If masses of cancer extend into the trunk of the hepatic vein, or if the hepatic vein of a single lobe be compressed by a neighboring carcinoma, these conditions will also lead to a stasis of blood in the portal vein and to ascites. These mechanical obstacles to free circulation in the portal vein, in frequent cases reach a degree sufficient to produce ascites only when the *vis a tergo*—the force of the heart—fails; for this reason the effusion frequently does not appear until the end of life approaches, and is then nearly synchronous with œdema of the extremities; although the cause of the obstruction, or compression, of the portal vein, has not increased.

The ascitic fluid has a specific gravity varying from 1,009 to 1,023, and contains 1 to 4 per cent. of albumen; it is sometimes limpid, light, or greenish yellow, sometimes is more icteric, and has a dark green or reddish brown color. More frequently it is cloudy, contains flocculi of fibrin, and, under the microscope, exhibits a multitude of white blood-corpuscles; the fluid thus presents the peculiarities of an inflammatory transudation, and in such case is usually richer in albumen. It frequently contains blood, which is generally the result of hemorrhage by diapedesis.

The effusions into the abdominal cavity often possess an inflammatory character, and sometimes from the very beginning; for a chronic inflammatory process, originating in peri-hepatitis, may extend over a large district of the peritoneum, and give rise to exudation; or, primarily, we have to deal with a passive effusion, which, through subsequent inflammatory processes in the peritoneal investment of the liver and its neighborhood, soon

assumes the character of an inflammatory exudation, and exhibits flocculent fibrin, wandering white blood-corpuscles, and an increase of albumen. An acute or subacute peritonitis, which hastens the fatal termination, may be called forth by perforation of a softened medullary node of the liver. If the perforation is the consequence of a severe hemorrhage in the cancerous masses, the peritoneal exudation will be hemorrhagic from the outset. Sometimes the effusion is purulent, especially so in chronic peritonitis after perforation of a softened cancer node.

Finally, chronic exudative peritonitis, in cancer of the liver, is sometimes cancerous from the beginning—that is to say, it is caused by a development of secondary cancerous nodes in the peritoneum. More frequently the carcinomatous peritonitis is primary, and the hepatic cancer secondary.

Here I wish to call attention to a circumstance which, apparently, is but little known, in connection with palpation of the liver during the presence of a collection of fluid in the abdominal cavity.

In well-developed ascites it not unfrequently happens, that, during a horizontal decubitus, the liver recedes from the anterior wall of the body and sinks backward, while the ascitic fluid interposes between the surface of the liver and the abdominal wall. In such cases, by a sort of ballottement, or palpation by a series of blows, we can feel the solid body of the liver through the overlying fluid.

Spleen.—In cancer of the liver the spleen is very seldom enlarged; a fact which is of value in the differential diagnosis between cancer and cirrhosis (also amyloid liver), but, of course, only when a decided enlargement of the spleen can be proven. In 116 cases reported by Hess and Frerichs, the spleen was enlarged in only 15. In hepatic carcinoma, enlargement of the spleen chiefly occurs, perhaps, when—the vascularity of the body and the amount of parenchyma in the organs being normal—numerous branches of the portal vein become destroyed by diffuse infiltration of cancer; or when there occurs an early extension of cancerous masses into the principal trunk of the portal vein, which is formed by the union of the superior mesenteric and splenic veins. The spleen, moreover, becomes enlarged in ex-

tremely rare cases, especially during diffuse cancer of the liver, in which it is secondarily affected by cancerous infiltration.

Pain.—The annoying sensations of dull pressure, of fulness in the abdomen, epigastrium, and hypochondrium, generally increase to severe pain at a later stage of the disease. In 55 cases, reported by Frerichs and Biermer, there were only 6 in which pain was not present during some period in the course of the disease. In many cases the pains reach an excessive degree, and palliation is effected only by large doses of opiates; in others the pains are insignificant, intermittent, and often absent for a long period of time. Budd has endeavored to explain the varying character of pain principally by the position of the secondary growths and the rapidity of their development. If the tumors are situated deeply in the liver, says this author, and enlarge slowly, pain is either absent or is insignificant; if, on the contrary, they approach the external surface, reach the peritoneum, and set up inflammation in it, the pain becomes acute.

This also occurs when, in consequence of a rapid growth of the tumors or of the entire liver, the serosa speedily becomes tense. The pains are most intense when the two factors—tension and inflammatory changes in the serous membrane—are combined. Budd's explanation is certainly justified in many cases; but we not unfrequently meet with exceptions, especially in those cases in which firm tumors of indolent growth, situated in the interior of the liver, are accompanied by severe pain.

Sometimes, also, intense suffering may be caused by inflammatory processes in the fissure of the liver (originating in cancerous swollen lymphatic glands of the portal fissure), involving the sympathetic and spinal nerves of this locality, which proceed from the cœliac plexus and accompany the hepatic artery (the spinal nerves in question coming through the splanchnic nerves).

Pressure upon, or percussion of, the liver often greatly intensifies the pain. Sometimes certain localities of the border or external surface of the liver, sometimes the palpable tumors, are constantly and especially painful under percussion and palpation.

Certain authors of earlier periods laid great stress upon the *lancinating* character of the pain of cancer in general, and

notably of carcinoma of the liver. This characteristic varies in the highest degree, and has no diagnostic significance.

In some cases, during the later periods of the disease, pain decreases or entirely disappears. This remission frequently coincides with the appearance of an abundant ascitic effusion.

The pain of cancer of the liver shares with abdominal pain, from other causes, the peculiarity that it radiates in various directions, and often to a great distance. The chief seat of pain is the region of the liver, the right hypochondrium, and the epigastrium; but cases have been described, in which, during the whole course of the disease, exquisite pain existed in the spinal, lumbar, and sacral regions, or in which pain in the right shoulder, in the right arm, right thigh, etc., coexisted with the pain in the liver. Widespread irradiation of pain to the lumbar, sacral, ischiatic, and femoral regions, naturally arouse a suspicion of the existence of a concurrent carcinoma of the retro-peritoneal glands.

The frequent irradiation of pain toward various portions of the body finds a partial anatomical explanation in the various sympathetic plexuses with their ganglia, which, together with others, are joined by the nerves of the liver and of its serous envelope. The ganglia of these plexuses represent, to a certain extent, lower centres, which very probably aggregate the irritation conducted to them by the nerves of *various* abdominal organs.

If we ask into which of these ganglia the nerves of the liver enter, the cœliac or solar ganglia are the first to be named. Emerging from these, the *hepatic* plexus (containing sympathetic and spinal nerve filaments) enters the liver with the hepatic artery. The left pneumogastric sends a branch of considerable size to the hepatic plexus, and accompanies it into the liver.

The nerves of the serous covering of the liver join the diaphragmatic plexus (an offshoot of the solar plexus), which receives sympathetic filaments, as well as those of the phrenic nerve. Moreover, filaments of the phrenic go directly to the serous envelope of the liver, and there terminate, as shown by Luschka,[1] who has thoroughly studied the ramifications of these nerve-tracts.

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[1] De nervo phrenico, Tübingen, 1853; also Anatomie d. Bauches, S. 245.

Since Romberg asserted that neuralgia of the brachial plexus is a frequent concomitant of various affections of the liver, and since Schoenlein has made the same claim with regard to pain in the right shoulder, too great stress, especially in former times, has been laid upon this kind of irradiation of pain in hepatic cancer.

Luschka explains the irradiation as a reflex irritation, which is conveyed from the spinal centre of one sensory nerve-tract to the neighboring centre of another. The phrenic nerve, a small portion of whose filaments terminate in the serous investment of the liver, anastomoses with the fourth cervical nerve, which sends sensitive filaments to the region of the shoulder (N. subcutaneus humeri). The irradiation or reflection of irritation, through the hepatic phrenic fibres to the cutaneous filaments of the fourth cervical nerve, may take place either in the spinal ganglion of the posterior roots or in the spinal cord itself. The anastomosis furnishes, to a certain extent, an anatomical guarantee for the theory that the spinal centres of both nerves lie near one another, and anastomose. Within a few years A. Spedl[1] has carefully studied the anatomical bearings of this subject. He discovered a considerable communication between the phrenic and fifth cervical nerves. Since the latter belongs to the brachial plexus, this anastomosis supplies further evidence of the connection between hepatic pain and brachial neuralgia.

Nutrition, Physiognomy, Changes in the Skin.

The patient emaciates — often with great rapidity. All the organs sustain a loss of parenchyma (especially the subcutaneous cellular tissue), and the emaciation occasionally is so extreme that the patient becomes almost a skeleton. The contour of the bones is especially evident and prominent in the face and on the head (squamous portion of temporal bone, orbital margins, the zygomata, etc.); also in the hand, thorax, at the elbows and knees, shoulders and vertebræ, in short, in those localities where no muscle or only a thin layer interposes between the bones

[1] Reichert's and Du Bois-Reymond's Archiv. 1872. S. 307.

and skin. A consequence of this disappearance of the subcutaneous cellular tissue is the spontaneous formation of folds in the skin, which are particularly noticeable in the face, as a deepening of the naso-labial furrows, and many others, which run parallel with these. The physiognomy thereby becomes essentially changed, and assumes that sharply outlined look which often leads us to suspect the existence of some cancerous affection. In our medical clinic I have seen numerous cases of cancer in which the weight of the body fell to an extremely low figure. A woman, fifty years of age, who had gastric and hepatic cancer, weighed (undressed) eighty-two pounds on entrance into the hospital. Three weeks later the weight of the cadaver was sixty-two and one-quarter pounds. This patient stated that two years previously she had weighed one hundred and thirteen pounds.

The chief source of the progressive emaciation, anæmia, and cachexia, undoubtedly lies in the imperfect renewal of the expended elements of the tissues—the insufficient supply of nutritive materials in consequence of anorexia—and the disturbed condition of digestion and assimilation. The more intimate nature of the process by means of which carcinoma effects these disturbances, as well as the influences which create the especial form of cancerous cachexia, are unknown. An *exact* and *thorough* study of the nutritive changes would throw much light upon the subject.

It is generally asserted that another factor takes an essential and decided share in the emaciation and cachexia, viz., the consumption of a large quantity of the albuminoid matters of the blood in the development of the cancerous growths. Budd has computed that a cancerous mass, five pounds in weight, which developed in five months, consumed the albuminous portion of twenty pounds of blood, and this computation is accepted by many as an adequate explanation of the cachexia and anæmia of cancerous patients. Of course, I will not deny that in their formation cancerous tumors absorb albuminous material from the blood; but it may be fairly supposed that within five months (!) the albuminous portion of twenty pounds of blood could easily be restored, and that this would indubitably be the

case if the digestive and assimilative processes of the patient continued undisturbed.

If fever develop, this consumption is not only increased and hastened, but the replacement of the waste is still more restricted.

Atrophy of the skin goes hand in hand with the loss of fat in the subcutaneous cellular tissue. The skin can be raised in long and high folds, which readjust themselves but slowly, and the elasticity of the cutaneous tissue is decreased; the latter has a peculiar dryness, loses its normal smoothness, often lies in fine folds, and exfoliates profusely (pityriasis tabescentium). The atrophied skin not only loses its normal smoothness, softness, and polish, but it experiences a change in color, and assumes a dirty gray, yellowish or brownish hue. In a similar manner the skin becomes discolored in very old age as a consequence of senile atrophy. But this discoloration of the skin is not always present. Many patients are extraordinarily anæmic, and show a pale, earth-colored skin.

On the other hand, we see an *icteric* discoloration of the cutis, of all shades, from a light yellowish tint to a deep lemon yellow and olive green—sometimes as a dark yellow brown (black jaundice). In cases in which it is doubtful as to whether the brown color is due to icterus or to atrophy of the skin, we should not neglect to examine the conjunctiva for icterus and likewise the urine. (See farther on.)

Jaundice of various degrees is a somewhat frequent phenomenon in cancer of the liver. But upon this point opinions are divided. Frerichs states that, in the majority of cases, icterus is absent; Budd and Murchison met with it "in a large number of cases." Uniting the statistics of these authors with those of van der Byl, Bamberger, and Biermer, we obtain 146 cases, in 67 of which icterus was present. It was therefore absent in about half the number of cases. In differential diagnosis jaundice is often of great value, especially when the question arises as to whether cancer of the liver has followed a carcinoma of the stomach, rectum, etc., which has already been diagnosticated; it is likewise useful in a differential diagnosis between carcinoma of the liver and of the stomach, or between cancerous and amyloid liver. If

icterus once makes its appearance in cancer of the liver, it becomes permanent, and is subject to no oscillations. (See below.) In the majority of cases the icterus of carcinoma of the liver originates in compression, or obstruction, of a large bile-duct or of numerous smaller ones. Cancerous nodes of the liver produce icterus, by compression of the biliary-ducts, so much the more readily when they are closely crowded in the neighborhood of the hilus of the organ. Occasionally masses of the tumor extend into larger bile-ducts, and act as obstructions. Budd, for example, reports a case of hepatic carcinoma, accompanied by intense jaundice, in which the cystic and hepatic ducts were gorged with cancerous matter.

Moreover, cancerously infiltrated lymphatic glands in the portal fissure may give rise to a stasis of the bile and to icterus, either through pressure or by a circumscribed inflammatory process, which results in the formation of constricting connective tissue. In a similar manner cancer of the stomach, of the head of the pancreas, or of the duodenum, may occasion a stoppage of bile and icterus, even when carcinoma of the liver does not exist. As an anatomical expression of the stagnation of bile, we not unfrequently meet with varicose, ampulla-shaped distentions in the hepatic biliary-ducts, or a multitude of cysts within the liver filled with bile.

The icterus of hepatic cancer originates exceptionally in other ways. Biermer[1] correctly affirms that in cancer of the liver, biliary calculi are of frequent occurrence; they were found in 16 cases out of 49. Biermer reports an hepatic carcinoma, attended by very pronounced icterus, in which a branch of the hepatic duct was plugged by a calculus. Unfrequently, icterus is caused by a catarrh of the large bile-ducts during carcinoma of the liver.

In the cases just mentioned, the icterus may exhibit fluctuations, and may sometimes entirely disappear. It is very obvious that many symptoms, such as pain and icterus, may undergo modifications through the complication of hepatic cancer with gall-stones.

Finally, I must not neglect to mention that in cancer of the

[1] *Hess*, loc. cit., S. 39.

liver, icterus is sometimes observed, and yet the post-mortem examination fails to reveal either compression or obstruction of the bile-ducts, or special signs of biliary stasis.

One of the consequences of jaundice in cancer of the liver, is an intense itching of the skin (pruritus cutaneus), which not only torments the patient in the highest degree, but obstinately withstands all treatment. The numerous effects of scratching, *i. e.*, excoriations in various localities of the cutis, are the objective expression of pruritis, especially noticeable in chronic icterus of long duration.

Urine.—When we are in doubt in regard to the existence of icteric or cachectic discoloration of the skin, the proof of the presence of bile in the urine is of importance. It is necessary repeatedly to examine the urine for bile, for sometimes it is present only temporarily, and at times entirely disappears. During the existence of strongly developed icterus, the appearance of the urine, its color, its intensely yellow foam, its power of coloration (when, for example, we test it with filter-paper), are all decisive. The various tests for bile all yield a positive result in such cases; the most simple being the Gmelin[1] test, over which, the more modern tests, particularly the modifications brought forward in recent years by Fleischl, Rosenbach, and others, do not possess the slightest advantage.

If the question is simply as to the presence of traces of biliary coloring matter, it often happens that none of the tests give a decided result; but even in such cases the Gmelin test, with some precautions, should be preferred.

Sometimes the urine no longer contains either bilirubin or biliverdin, but only biliprasin. In this event Huppert's test (*vide* Neubauer and Vogel's Urinary Analysis) has repeatedly given me a beautiful and positive result, particularly when none of the other tests were able to prove the presence of bile pigment in the urine.

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[1] Into a test tube pour a small quantity of the urine to be examined; carefully add an equal quantity of strong nitric acid which contains a little hyponitric acid. Two layers of fluid will form, at the junction of which, in case bile be present, will appear a zone of colors, viz.: green, blue, violet, red, yellow, which arrange themselves in the order mentioned, the latter color being the highest in position. Green predominates; the blue tint is often absent. (*Ultzmann* and *Hoffmann*, Harn-Analyse).—TRANS.

In carcinoma of the liver, the urine at times contains a profuse quantity of indican. But since increase of the indigo-forming substance in the urine occurs in the most dissimilar diseases (I have found it in considerable quantities in cancer of the stomach, gastric dilatation, benign stenosis of the pylorus, gastric ulcer, chronic dysentery, chronic pleurisy with exudation, chronic peritonitis, in a case of lead colic, and, a few days ago, in the urine of a patient convalescent from typhoid), it may be said that the evidence of abundance of indican in the urine has no pathognomonic significance[1] in cancer of the liver.

In pigment cancer of the liver, still other not well-known coloring matters appear in the urine, notably a pigment which becomes black by oxidation on exposure of the urine to the air, and on addition of nitric acid (melanin, melanuria). Ganghofer, Pribram,[2] Stiller, and Lench, found this pigment in pigment cancer; I have also seen it in unpigmented, simple medullary cancer of the stomach and liver. In a case of gastric cancer, which came under my notice, the urine, spectroscopically examined by Vierordt, was extraordinarily rich in indican. It was strikingly dark, even blackish brown, in color, and upon the addition of HNO_3 became quite black. The formation of an abundance of indican[3] probably concurs in all these cases with the appearance of this black pigment (phenol).

In intense icterus of long duration, a small quantity of albumen will usually be found in the urine. The presence of leucin and tyrosin, in the urine of patients suffering from hepatic cancer, is extremely rare. In a case of multiple adenoid nodes of the liver, Griesinger[4] found both these substances in the urine.

It appears that the deposition of bile pigment in the kidneys, and its passage through the uriniferous tubules, acts as an irritant and causes desquamation of epithelium. This is the simplest manner of explaining those cases of uncomplicated catarrhal

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[1] In regard to the qualitative and quantitative proof of indican, see the Lehr. d. phys. Chemie, von *Hoppe-Seyler*, *Neubauer* and *Vogel*, *Loebisch*. For the spectroscopic determination of the quantity of indican, see *Vierordt*, Zeitschr. f. Biolog., X. Bd., S. 27.

[2] Prager Vierteljahrschrift. 1876. CXXX. S. 77.

[3] For details by *Salkowsky*, see Centralblatt d. med. Wissensch., 1876, No. 46.

[4] Archiv d. Heilk. 1864. 1. Jahrgang. S. 385.

jaundice in which casts and traces of albumen are found in the urine.

The deposition of bile pigment in the kidneys sometimes gives rise to a very gradual interstitial nephritis, and leads to icteric pigmentary induration of these organs. In other cases of well-developed and permanent albuminuria, there is a complication with parenchymatous degeneration of the kidneys (Bright's disease). In twenty-four cases of cancer of the liver, Biermer found this affection of the kidneys in only one instance.

The total *quantity of urine* in the twenty four hours is often less than normal, especially on the appearance of abundant ascites, or during the existence of fever; also toward the end of life, when the cardiac power sinks and œdema arises; finally, when profuse diarrhœa or frequent vomiting is present. The well-known fact should here be mentioned, that after paracentesis and evacuation of the ascitic fluid, the quantity of urine often increases. The daily amount of the chlorides and urea is usually decreased in accordance with the deficiency in the absorption and assimilation of nutriment and with the loss in the weight of the body.

Circulation and Blood.—The actual quantity of the blood diminishes in conformity with the emaciation of the body; the relation between the weight of the latter and that of the blood remains nearly the same.

We have but slight knowledge of the qualitative changes in the blood. Thanks to the improvement in methods of examination, the greatest attention has been paid to the hæmoglobulin of the blood. I am able to give some information in regard to this subject, upon the strength of many examinations which I have made of the blood of cancerous patients. A decrease in the amount of the hæmoglobulin occurs, which, in general, is more or less considerable, according to the duration of the disease and the degree of the cachexia. In *extreme* cases the proportion is about fifty to sixty per cent. of the quantity of hæmoglobulin in the blood of a healthy person.

An interesting fact which I discovered, in examining this substance by Vierordt's method, is that toward the close of life the relative amount of hæmoglobulin in the blood of cancerous

patients (especially in gastric and hepatic cancer) sometimes rapidly increases, and even exceeds the normal quantity.

This interesting phenomenon may be observed at a time when the patients, who have, to a certain degree, become dried and mummified, are gradually dying with symptoms attributable to decrease in the watery portions of the blood and of the parenchyma of the organs.

The dryness of all the tissues and the tarry nature of the blood in such cases have long been familiar to the pathological anatomist. During life they find their expression in an increased quantity of hæmoglobulin in the blood.

The decrease of this element of the blood, in patients who are suffering from cancer of the liver, gives rise to many phenomena analogous to those observed in chlorosis. Among these, in addition to a conspicuous anæmia of the cutis and mucous membrane, are shortness of breath upon slight exertion, a tendency to syncope, palpitation, and irritable heart. The latter shows itself in a decided acceleration in the frequency of the pulse on moderate activity of the body. The rapid exhaustion and the incapacity for physical exertion are also partly due to the pathological condition of the blood; in part, also, to actual loss of muscular substance.

Toward the close of life, in consequence of cardiac atrophy, the signs of deficient (retarded) circulation become apparent, viz., œdema in the inferior extremities, and the formation of thrombi in the crural and popliteal veins. The œdema of the legs is often favored by the pressure which the ascites, or the enormously enlarged liver, exercises upon the inferior vena cava. After paracentesis abdominis and evacuation of the ascitic fluid, the œdema sometimes disappears.

In these cases of retardation of the blood in the inferior vena cava, the superficial epigastric vein (abdominalis subcutanea) is sometimes distended with blood ; the cutaneous branches of the superior epigastric and long thoracic veins, which communicate with the superficial epigastric, are also dilated at times.

A thorough microscopic examination of the blood of cancerous patients often yields results which, while not especially characteristic of cancer, are, nevertheless, worthy of careful

study. In numerous instances the red blood-corpuscles exhibit no abnormal change in either their size, form, or color. In others a certain, though not a high, degree of variety of shape (poikilocytosis) exists. Beside the red blood-corpuscles of normal size (7–7.5 μ in diameter), we find smaller corpuscles, measuring 6–4 μ in diameter, and here and there a giant blood-corpuscle (*globule géant*, Hayem), or a "microcyte," in the sense adopted by Masius and Vanlair—that is to say, a blood-globule somewhat dark in color, perfectly globular, not bi-concave, and having a diameter of 4 μ. Moreover, in the blood of cancerous subjects I repeatedly have found granular débris of *white* blood-corpuscles, as first described by Riess,[1] and also the granular products of disintegrated *red* blood-globules.

The latter present themselves in the shape of small, globular, perfectly homogeneous bodies, having a diameter of about 1–3 μ, and a strong refractive power. In tint they are sometimes reddish, or of a greenish yellow color, resembling the hue which the red blood-corpuscles assume when they are exposed to the action of water.

The *cardiac sounds* are clear ; an accidental systolic murmur may frequently be heard at the apex. Sometimes, in consequence of the thinness of the thoracic walls from loss of fat and muscle, the sounds of the heart are very loud and ringing. In some cases, as a result of shallowness of respiration and the limited *besoin de respirer*, the borders of the lungs become retracted. In this event, in spite of the atrophy of the heart, cardiac dulness is larger than normal, especially in a vertical direction along the left border of the sternum; and during the heart's impulse systolic pulsations are evident, not only at the apex of the heart, but likewise near the sternum, in the fourth and even the third interspace.

When jaundice is well pronounced, the action of biliary acids upon the heart is made evident by a sluggishness in the cardiac movements.

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[1] Reichert's und Du Bois-Reymond's Arch. 1872. S. 244.

Gastro-Intestinal Symptoms.

Dyspeptic symptoms of various kinds, viz., loss of appetite, vomiting, etc., irregularity in defecation, and temporary tympanites, are commonly initial symptoms of cancer of the liver, which usually become intensified with increase in the cachexia.

We are unable to give an adequate explanation of these initial disturbances in the gastro-intestinal functions, which play a rôle of such importance in the origin of the cachexia. Changes in the functions of the liver, qualitative anomalies, or deficient secretion of the bile, and consequent disturbances in digestion, especially the digestion of fat, are usually given a first rank in explanation of the phenomena which I have mentioned; but these are unproven hypotheses.

At a later period, when the hepatic cancer has led to a stasis in the portal vein, the symptoms of dyspepsia and the disturbances in the intestinal functions are probably due in part to the diffuse catarrh which has been created by passive congestion.

Even when the cancer is only present in the liver, obstinate vomiting sometimes exists during the whole course of the disease. This symptom is often called "consensual," and "sympathetic," or it is supposed to be due to the pressure of the enlarged liver upon the pylorus, whereby, to a certain degree, a stenosis by compression is created. I do not believe in the efficiency of such a pressure. On the other hand, stenosis may be produced by constricting adhesions of the pylorus in the concavity of the liver, or by kinks or distortions in simple adhesions. A similar effect is produced when the pylorus is surrounded by cancerous lymphatic glands in addition to the adhesions. In many cases the emesis is actually consensual, that is to say, in the language of the physiologist, it is a reflex effect of irritation of the peritoneum or of the hepatic nerves, especially of the capsular branches.

In cases of uncomplicated carcinoma of the liver, accompanied by obstinate vomiting, when the *general* symptoms of the cancerous affection are alone apparent, when the liver is not enlarged, when there is no evidence of the existence of a tumor, and when

no jaundice is present, it is very evident that the diagnosis might easily take a wrong direction, and would probably be cancer of the stomach. Autopsy proves the error. On the contrary, in gastric carcinoma, emesis often entirely fails to appear; no tumor can be felt at the pylorus; if, in such a case, secondary cancer of the liver, with enlargement and palpable nodes in the organ, were present, the diagnosis probably would be that of primary hepatic carcinoma, and the actual and primary seat of the disease would be overlooked. Such errors cannot be avoided.

Obstinate constipation, with its sequelæ, is frequently an attendant symptom of hepatic cancer. The passive congestion in the intestinal walls creates a weakness in the functions of the intestinal muscular fibres, and the peristaltic action becomes slower. A similar effect arises from changes in the mucous membrane through chronic catarrh (diminished sensibility); perhaps also from a deficiency of bile in the intestines.

Through obstructions to the flow of the biliary secretion into the bowels, the *fæces become colorless, gray, clayey, fatty;* they putrify and diffuse a putrid, carrion-like odor. During the last weeks of life obstinate diarrhœa sometimes sets in, and hastens the fatal termination. In such cases the autopsy reveals follicular ulcers in the large intestine, hemorrhagic infiltrations of the mucous membrane in places, and superficial diphtheritic necrosis, especially along the free borders of the mucous folds.

If the stasis of the portal blood attains a high degree, as in cirrhosis, it may give rise to *gastric and intestinal hemorrhages.* This is a very rare occurrence in cancer of the liver, and, under special conditions, essentially increases the difficulty of a differential diagnosis between hepatic carcinoma, on the one hand, and gastric cancer or cirrhosis on the other.

Hemorrhoidal swellings are not rare, and the rupture and hemorrhage of a hemorrhoid is looked upon by the patient as an important indication of improvement.

Respiration.—I have already made reference (S. 389) to the dyspnœa on exertion dependent upon the anæmia of the patient. Upward dislocation of the diaphragm by an enlarged liver, or as a consequence of ascites or meteorism, gives rise to more or less

severe dyspnœa, and causes a livid discoloration of the lips and prominences of the features.

Symptoms of *dry pleuritis* make their appearance when cancerous nodes, or the inflammatory processes which they have created, spread to the diaphragm, and thence to the diaphragmatic, pulmonary, or costal pleura.

Hemorrhagic transudations and pleuritic effusion into the right pleural cavity are not unfrequent consequences of cancer of the liver. *Empyema* also has been observed, especially when a softened cancer node has broken into the pleural cavity of the right side.

Secondary cancer of the pleura, the lungs, or the mediastinal or bronchial lymphatic glands, is rare.

Hypostasis of various degrees in the lower lobes of the lung, pulmonary œdema, and croupous pneumonia often make their appearance toward the close of life.

Fever.—In the majority of cases the disease runs its course without any signs of fever. The temperature of the body, especially toward the end of life, is often lower than normal. According to Frerichs, the reason may lie in the parenchymatous atrophy in all the organs and in the coexisting anæmia. In consequence of these conditions, the sum of the disassimilative processes of the economy sinks to a low ebb, and production of heat is less active, while the factors in the radiation of heat are not restricted to the same extent. Hess thinks that the icterus may also act as a cause of the subnormal temperature, since it also causes retardation of the pulse. A retarded circulation will readily explain the coolness of the skin and extremities, but not the depressed temperature of the internal organs. Moreover, it is a mistaken opinion to believe that the circulation is retarded synchronously with a decrease in the frequency of the pulse.

Frequent and long-continued observations of the temperature teach us that perfectly atypic and sporadic exacerbations of fever make their appearance in many cases of hepatic carcinoma independently of the stage of the disease. There are exceptional cases in which, from beginning to end, cancer of the liver is accompanied by fever. The latter for a long period may be a continued fever, with morning remissions and evening exacerba-

tions; more frequently it has a hectic character, and is accompanied by night sweats. Fever also regularly appears when peritonitis, pleuritis, necrosis, and decomposition of cancerous masses, pylephlebitis, thrombosis of the crural veins, croupous pneumonia, and other complications occur.

Nervous Symptoms.—I have already stated that pain is an almost constant symptom of cancer of the liver.

As in many other chronic abdominal diseases, the mood of the patient becomes depressed. He is irritable and sensitive, downcast, hopeless. The sleeplessness, pains, the enduring sense of weariness, and the incapacity for physical or mental activity, increase the mental distress. At a later period a more indifferent apathetic mood frequently appears, often with the signs of psychical weakness, as loss of memory and of the previous powers of judgment. In some cases we see a reviving mood near the close of life, an awakening of new hopes, and the resulting plans for the future.

The physical weakness is characterized by the gait of the patient, by the tremor, especially in the hands, and by the weak, non-resonant voice.

Singultus—a symptom which often torments the patient in the highest degree—is frequently observed.

A soporific condition, resulting from cerebral œdema, develops in many cases toward the close of life.

When a pronounced jaundice exists, death sometimes occurs—with the symptoms of cholæmia—during the deepest stupor, after the occurrence of active delirium with convulsions.

Lymphatic Glands.—The lymphatic glands offer us no assistance in forming a diagnosis of hepatic cancer, excepting in extremely rare cases, *e. g.*, in melanotic cancer of superficial glands. An undeserved importance is given by many to a swelling of the jugular lymphatic glands (situated just above the left clavicle). I have examined very many cancerous patients in regard to this point, but the results were unfailingly negative. The enlargement of the inguinal glands has also been considered a valuable diagnostic symptom. The physician, however, should be on his guard against diagnosticating carcinoma of these clusters of glands, because of their distinct prominence, since this may be

the consequence of emaciation or of œdematous swelling from stasis.

Differential Diagnosis.

The diagnosis of cancer of the liver can be determined from the symptoms I have cited, and in the delineation of which I have repeatedly alluded to the anomalies of individual signs and to their importance in differential diagnosis.

The question as to which form of cancer is present, whether it be carcinoma simplex, indurated, medullary, cystic, alveolar, melanotic, or adeno-carcinoma, whether it be sarcoma, etc., is a question which can be answered during life only in the rarest cases. *Intra vitam* we must satisfy ourselves with the diagnosis: *malignant neoplasm of the liver.* The more intimate anatomical differences are often first revealed by the microscope. Only in those cases of hepatic cancer in which a melanotic carcinoma—proceeding, for example, from the choroid—is present, or upon which an operation has been performed years before, or where a determined form of cancer of the external soft tissues has been recognized, as an alveolar cancer of the rectum, or a sarcoma (*e. g.*, epulis),—only in such cases, and from the recognized nature of the visible primary cancer, can we feel certain that the growth in the liver is of a similar nature.

In many cases, in which all the symptoms of cancer of the liver are evident, the question is raised, Is this a primary or a secondary growth? The answer is not difficult, if we can prove the presence of a *larger* cancerous mass in some other organ. Under such conditions we should hardly ever err in supposing the hepatic cancer to be secondary. The lungs and pleuræ are, however, often secondarily affected from cancer of the liver; and sometimes we find a secondary mediastinal carcinoma; or—and this is usually first discovered during the autopsy—there may be *small*, isolated centres of cancer in the peritoneum or omentum, in the portal or retro-peritoneal lymphatic glands; these indisputably are the consequence of a primary hepatic cancer. It must not be forgotten that primary carcinoma—of the stomach, for example—may develop slowly, while the secondary hepatic

cancer proliferates and spreads with great rapidity. In such case the primary growth seems insignificant, as compared with the much greater development of the secondary neoplasm.

Occasionally only the symptoms of cancer of the liver are evident, and the latter seems to be primary; and yet a primary point of origin exists in some other organ, *e. g.*, latent gastric carcinoma; or there is a latent primary carcinoma of the retroperitoneal or portal lymphatic glands, of the gall-bladder, the pancreas, mediastinum, vertebræ or other bones, of the mesentery, peritoneum, intestines, one of the ovaries, etc.

But, on the contrary, it sometimes happens—yet much more unfrequently—that, when a cancer of the liver has been diagnosticated, many symptoms, such as frequent vomiting, hæmatemesis, or bloody fecal discharges, seem to indicate a primary cancer of the stomach, while the hepatic carcinoma proves to be primary.

Finally, when the existence of cancer of the stomach, peritoneum, mammæ, uterus, ovaries, etc., has been confirmed, it often happens that all appearances, by means of which a coexisting hepatic tumor might be diagnosticated, completely fail, and nevertheless the autopsy reveals one or even several cancer nodes in the liver.

Sometimes the question arises as to whether hepatic cancer be present or gastric cancer; whether cancer of the liver, or cancer of the colon, omentum, or even of the right kidney. This doubt arises when the symptoms by which one or another of these affections can be diagnosticated with certainty are inadequate, especially when the tumor is so situated that it is impossible to determine whether it springs from the liver or the gall-bladder, or is connected to either organ by contiguity or by direct and intimate adhesions. The difficulty of establishing a positive diagnosis is often only temporary, for at a later period the symptoms become clearer, and a definite diagnosis is made possible.

I have already shown that, in extremely rare cases, a latent cancer of the liver, attended by constant febrile symptoms, may run its course under the guise of a chronic right-sided pleuritis, with effusion (supposed to be tubercular), or of peritonitis.

Of those diseases of the liver which may be mistaken for he-

patic carcinoma, and *vice versa*, I wish to render the following conspicuous:

1. *Multiple Adenoid Tumors of the Liver.*—In common with cancer of the liver, they have the following symptoms, viz.: considerable enlargement of the organ, perceptible nodular protuberances and tumors, icterus, ascites, etc. On the other hand, in adenoma the vigor of the patient is retained longer, the cachexia develops slowly, and never in the form of the genuine marasmus of carcinoma. The course of the disease is more prolonged; in the interesting case described by Griesinger[1] it continued for a space of two years.

During life, adeno-carcinoma can in no way be distinguished from carcinoma.

2. *Diffuse Adenoma of the Liver.*—For a long time I had the opportunity, in Lindwurm's clinic, of watching a case of this nature in a young man between twenty and thirty years of age. The symptoms present were enormous enlargement of the liver—but without palpable tumors—intense jaundice, decided hypertrophy of the spleen, and, later, ascites. The disease lasted a little more than two years. Our diagnosis was that of multilocular echinococcus. An anatomical examination by Buhl showed that the disease was diffuse adenoma of the liver.

3. In *chronic obturation of the gall-ducts* by biliary calculi, or in the resulting inflammation and contraction of Glisson's capsule in the neighborhood of the biliary ducts which lie in the portal fissure (and become obliterated), there may arise a combination of symptoms which present great similarity to those of hepatic cancer. The liver is enlarged; at a later period it becomes smaller. Through cystic distention of the bile-ducts, protuberances may become perceptible on the surface of the organ. Intense icterus appears, and the patient emaciates to the highest degree. In a case which I saw in the clinic at Munich, and which finally was brought to the autopsy-room, the prolonged course of the disease and previous attacks of gall-stone colic, etc., rendered the diagnosis certain. In Murchison's

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[1] Arch. d. Heilkunde. 1864. 1. Jahrg. S. 385. See *Rokitansky*, Wien. allg. med. Zeit. 1859. S. 98.

wards in St. Thomas's Hospital, in London, I saw a perfectly similar case: the long duration and previous attacks of gall-stone colic excluded carcinoma; but, at first glance, the high grade of marasmus and the hard, localized, nodular condition of the liver suggested cancer.

4. In *chronic adhesive pylephlebitis*, especially that form in which the obliteration of the portal vein is limited to certain hepatic branches, and gives rise to a partially lobular, knobbed condition of the liver (Frerichs, loc. cit., S. 374), the symptoms, under certain conditions, and when the strength of the patient rapidly fails, may lead one to confound the disease with carcinoma. In regard to the diagnosis of the affection under consideration, I may refer my readers to the chapter on Thrombosis and Obliteration of the Portal Vein, in this work.

5. As proven by the case related by Frerichs (S. 117), *abscess of the liver* sometimes runs its course under symptoms so vague that a diagnosis of this condition may be impossible. Moreover, since in hepatic cancer irregular febrile movements, exhibiting perhaps even a hectic type, are sometimes observed, palpable tumors not being by any means always present, a confusion between cancer and abscess naturally may occur in exceptional cases — especially so because, in case of abscess, the emaciation and marasmus frequently make very rapid progress. This error is equally liable to arise when the diagnosis lies between abscess and soft, fluctuating hepatic cancer of rapid growth. In abscess chills are frequent; in cancer very rare. In the majority of cases of abscess, icterus is not present, and never reaches such a high degree as in *many* examples of cancer. In a great number of instances the etiology is decisive of one affection or the other.

6. *Cirrhosis.*—In cancer of the liver, if no large, nodular protuberances are perceptible; if the cachexia is of slow development; if there are no symptoms of cancer in some other locality —for example, in the stomach; if there is a history of intemperance; and if, exceptionally, gastric or intestinal hemorrhages occur, the diagnosis of cirrhosis may very readily be made; and if, on the other hand, in cirrhosis the liver enlarges, and there is no hypertrophy of the spleen; if intemperance cannot be proven, and there is rapid loss of strength, and the patient

quickly emaciates—under these conditions the differential diagnosis between cancer of the liver and cirrhosis occasionally becomes very difficult, or even impossible. In most cases the further course of the disease leads to a correct diagnosis. In diffuse, infiltrated cancer of the liver the surface of the organ may present a great similarity to a granular liver. (See the section on Pathological Anatomy, by Schueppel.)

7. *Hydatid and Multilocular Echinococcus Tumors.*—The *hydatid echinococcus*, exceptionally, may run a latent course in so far that the liver is enlarged, or that a flattened protuberance is formed; but, under these conditions, it never gives rise to a large, fluctuating cyst accessible to palpation. In such a case, however, the *duration of the disease* and the absence of the cancerous cachexia positively exclude hepatic carcinoma; and, further, if a large cyst be present, or if the examination by puncture reveal the absence of albumen in the fluid contents and the remaining characteristics of the echinococcus, no error is possible.

The *multilocular echinococcus* tumor, of which I have seen, *intra vitam*, two beautiful and correctly diagnosticated examples, presents symptoms which much oftener render it similar to cancer of the liver. Hard, globular tumors make their appearance, which afterward become softer and larger. The liver is markedly increased in size. The patient is generally extremely jaundiced. In opposition to cancer of the liver, in which enlargement of the spleen is extraordinarily rare, the hypertrophy of this organ is an almost constant symptom in multilocular echinococcus. Moreover, in most cases, the duration of the disease —two, three, or more years—and the absence of the genuine cancerous marasmus, exclude hepatic cancer. The age of the patient often speaks more in favor of one than the other of the two diseases in question.

8. A *confusion* of cancerous with amyloid liver is hardly possible for any length of time. The indolent course of the affection, the absence of the cancerous cachexia, the smooth surface of a hard, enlarged, amyloid liver, the coexisting amyloid degeneration of the spleen, the albuminuria, and, finally, the etiology of waxy degeneration, exclude the possibility of an error in diagnosis.

9. The *syphilitic liver*, on examination, may present the greatest similarity to a cancerous one, especially when the nodes are not easily recognized, but give the impression of being flat protuberances rather than genuine nodular formations. But the prolonged duration of the disease, the etiology, the absence of the true cancerous cachexia, the evidence of other symptoms of syphilis (cicatrized pharyngeal ulcers, etc.), in most cases secure a correct diagnosis, and especially when the spleen and kidneys, at the same time, give evidence of amyloid degeneration. A corset-lobe of the liver, or collections of fæces in the ascending or transverse colon, will lead only the very inexperienced to mistake them for carcinoma for any length of time. A liver enlarged by passive congestion (in cardiac and pulmonary ailments, or in large pleuritic effusions, etc.) should hardly ever lead one into the error of mistaking it for a cancerous liver.

I cannot close this discussion of the differential diagnosis without mentioning an aid which may often be of value in doubtful cases. I refer to the *weight* of the body. In a great number of cases, when the absence of all objective symptoms on the part of liver or stomach leads us to doubt whether the evidences of dyspepsia and emaciation depend upon a latent gastric or hepatic carcinoma, or whether they are due to a chronic gastric catarrh, repeated comparisons of the weight of the patient sometimes give us a point of departure in forming a diagnosis.

If, by means of a rational diet, we succeed in increasing the weight of the body of the patient, even in a slight degree, we are, in all probability, justified in excluding carcinoma, in spite of the fact that the appearance of the patient has not yet improved. By weighing the cancerous patients of the Tübingen clinic, in very numerous instances, I have been able to prove an unexceptionally progressive loss of weight. Increase in weight in carcinoma is observed only when œdema, ascites, or hydrothorax sets in, signs which tell us that the parenchyma of all the organs is beginning to be richer in water. On the contrary, I do not know of a single case in which a rapid enlargement of the liver has increased the weight of the patient.

Duration.

The impossibility of establishing the date of the *beginning* of the disease, by means of information gathered from patients, renders the opinions which I have been able to collect concerning the duration of the disease only approximately correct. We meet with cases in which chronic disturbances of digestion, hypochondriasis, and symptoms of dyspepsia precede cancer of the liver for a long period of time. Since the commencement of the cancer has often been dated from the appearance of the first evidence of indisposition, certain authors have been led into the error of considering the duration of individual cases to be that of several years.

Estimates of the medium or average duration of cancer of the liver differ very widely. As a means of deciding the question, I may add six cases of the Tübingen clinic to those selected from the statistics of Frerichs and Murchison, 19 cases in all, whose total duration was 378 weeks, making an average of 20 weeks. The average duration of 25 cases, which were analyzed with the utmost care by Biermer, was 17 weeks. Those which exceed one year in duration are, to say the least, extremely rare; and the assertion of Bamberger, that "the course of cancer of the liver often covers a period of several years," I consider erroneous. *Perhaps* the cases of abnormally long duration may have been primary adenoma, which only at a later period became converted into adeno-carcinoma.

In rare instances cancer of the liver runs a fatal course in from four to eight weeks, under the guise of an *acute* hepatitis, with permanently high fever and rapid emaciation. Biermer saw a case of five weeks' duration; Frerichs one of only four weeks' duration; Bamberger one which ran its course in eight weeks.

Especially interesting is a case related by Bamberger (loc. cit., S. 606). A previously healthy man, forty-eight years of age, was suddenly attacked by intense pain in the hepatic region, attended by well-marked jaundice and high fever. Moderate delirium, difficult respiration, and occasional singultus, soon followed. The liver was very painful, and became enlarged, but showed no irregularities on palpation. Chills and bloody stools made their appearance. Under a constant and intense fever, rapid emaciation, collapse, and coma, death occurred eight weeks

after the initiation of the first symptom of illness. *Autopsy.*—In addition to numerous deposits in the liver, there was found a softened medullary sarcoma, which had entirely destroyed the gall-bladder and perforated the duodenum.

In general the duration of the disease is shorter, and its course more rapid, according as the nodes, which establish themselves in the liver, are more numerous; and the more rapid their growth so much the earlier do they become softened and converted into an ichorous fluid. For that reason scirrhus runs a longer course, on the whole, than medullary cancer. It is self-evident that the duration depends upon the history of the hepatic cancer, viz., as to whether it be primary, or whether it be secondary to long-developed carcinoma of some other organ.

Finally, the course of the lesion is often essentially shortened by an intercurrent right pleuritis, by pneumonia, by perforation into the abdominal cavity and peritonitis, by hemorrhages in softened cancer nodes, or into the abdominal cavity, likewise by fever, diarrhœa, obstinate vomiting, etc.

Termination and Prognosis.

Under all conditions the prognosis is fatal. Supported in their views by the retrogressive fatty changes which the cancerous nodes of the liver often present anatomically, supported too, especially, by the dense cicatricial masses which are found in the midst of large cancer nodes, and which cause the depression of their centres, Oppolzer, Bochdalek, and Henoch, as is well known, claim that by means of these processes the cure of cancer is possible.

The case which Bochdalek asserted was one of recovery from cancer of the liver, proved to be a syphilitic, lobulated liver, as Dietrich has since shown. Oppolzer and Henoch have rescinded their views. Fatty degeneration of the cancer-cells, and the formation of cicatrices in the centres of the cancer nodes, may, indeed, be considered a curative process in individual nodes, but they never lead to a cure of hepatic cancer, because fresh elements of the neoplasm *always* appear in the neighborhood of nodes which are undergoing fatty degeneration and contraction, and these develop into new tumors.

The fatal termination occurs in various ways. Sometimes, in a constantly increasing marasmus, the patient, after being in a moribund condition for days, dies of exhaustion. The weakness becomes extreme, the movements grow feebler, the voice becomes toneless, whispering, and exhausted; the patient lies motionless, and has the appearance of a mummy; the eyes are deeply sunken, surrounded by dark circles, and stare with a peculiarly dull gleaming look; the respiration is superficial and slow; the tongue is dry and leathery; the extremities cold; the pulse small and threadlike.

In many of these cases resorption of water from the intestinal canal, perhaps in consequence of deficient peristaltic action, seems difficult. On post-mortem examination the cadaver is found to have the appearance of a victim of cholera; most of the tissues, especially the muscles and subcutaneous cellular tissue, are surprisingly dry; the blood is black and of tarry consistence (see p. 389). When auscultating the hearts of certain of these patients I have detected a soft pericardial friction murmur; and my supposition, that it was due to dryness of the pericardium, was justified by the revelations of the autopsy.

In other cases, toward the end of life, œdema of the lower extremities sets in, likewise ascites, giving rise to great dyspnœa, venous thrombi form in the crural or popliteal vein, etc. Death is finally caused by pulmonary œdema.

Death sometimes occurs suddenly from a fatal increase of cerebral anæmia, especially during a quick change of posture from horizontal to upright.

The fatal end is occasionally hastened by a rapid increase of anæmia from hemorrhages which ensue in softened cancerous growths. A quick enlargement of the liver, with symptoms of great anæmia, are signs frequently diagnostic of hemorrhage. In other cases the extravasation causes rupture of the cancer nodes; this is followed by a flow of blood into the abdominal cavity, or between the liver and diaphragm, or, by rupture, into the right pleural cavity.

The perforation of a softened or diffluent mass of cancer into the peritoneal or pleural cavity is followed by a fatal peritonitis or pleuritis.

Toward the close of life a well-marked *hemorrhagic diathesis*, indicated by small but innumerable hemorrhages in the most dissimilar organs, becomes developed, especially in those cases in which there exists a high grade of icterus. In consequence, we find bleeding from the nose, the gums, the soft palate, numerous petechiæ in the skin, ecchymoses in the serous membranes, extravasations into the mediastinal or retro-peritoneal cellular tissue, hemorrhagic effusions into the pleural and peritoneal cavities, etc. In a case of multilocular echinococcus which came under my observation, the hemorrhagic diathesis gave rise to a fatal hemorrhage in the cerebral meninges and in the subarachnoid space of one hemisphere. Sometimes, especially when the jaundice is intense, death ensues from the so-called "cholemic intoxication," after previous convulsions and delirium, attended by high fever and coma.

Cerebral œdema and anæmia of the brain may be mentioned as frequent causes of death. Croupous pneumonia is also sometimes the immediate cause of the fatal termination.

Treatment.

The treatment of cancer of the liver has no other object than to preserve the strength of the patient for the longest possible time, and to ameliorate and overcome the pains, and lessen the discomforts connected with the disease.

The first duty—that of nourishing the patient—can never be perfectly accomplished; the marasmus is progressive, and cannot be checked. The only thing we can achieve, by a wise choice of articles of food (milk, meat—especially scraped raw beef, which is very easily digested), and by such tonics and appetizers as quinine, rhubarb, and strong wines, is to delay the loss of strength.

The annoyances which arise from irregularities of the intestinal functions, viz., constipation, meteorism, diarrhœa, etc., may be combated by the usual means. Dyspnœa resulting from ascites can be overcome with the greatest certainty by the help of the trocar.

In the treatment of sleeplessness, pain, singultus, and pruritus of the skin, opium and chloral hydrate occupy the first rank.

Amyloid Degeneration of the Liver;

Fatty Liver; Pigment Liver.

SCHUEPPEL.

AMYLOID DEGENERATION OF THE LIVER.

(Lardaceous or Waxy Degeneration—Lardaceous Liver—Waxy Liver.)

Literature.

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The higher grades of amyloid degeneration of the liver cause such gross, and, at the same time, such characteristic changes in this organ as to justify the presumption that these could not have escaped the notice of the earlier physicians. And, indeed, the medical works and post-mortem reports of our predecessors contain descriptions from which we may with great certainty deduce the diagnosis of amyloid liver. We learn, from the same sources, that the older physicians supposed the amyloid liver, as well as various other changes accompanied with enlargement of organs, to have been brought about by the deposit of some for-

eign substance; inasmuch as the expressions used to designate these conditions, such as obstruction, infarction, physconia, etc., are based upon the idea that diseased inspissated juices clogged the vessels of such organs and were deposited there. Such indefinite, and, in part, erroneous, suppositions prevailed for a long time. It is to the credit of Rokitansky that he gathered together in one picture—which was correct in its principal features—the anatomical characteristics of organs subject to amyloid degeneration, especially those of the liver and spleen; while, at the same time, he established the genetic connection of amyloid degeneration with certain cachectic conditions.

For a long time opinions differed greatly concerning the chemical nature of the material deposited in organs which are the seat of amyloid degeneration. One party, influenced by the physical appearance of the material, were content to compare it to lard (lardaceous liver), and this was especially true of the Vienna school; while another party thought it might be more appropriately compared to wax, and accordingly spoke of waxy degeneration of the liver. The latter was especially true of England, following the example of the Edinburgh school. Others, again, regarded the substance in question as falling within the very indefinite scope of the term "colloid," and adhered to the expression colloid liver. Amongst this number were Oppolzer, Schrant, and others. Budd treats of amyloid liver under the designation of scrofulous tumor of the liver.

Systematic progress in the investigation of amyloid disease was first rendered possible by the disovery, on the part of Virchow, in the year 1853, of the peculiar reaction of the substance in question with iodine and sulphuric acid. He soon afterwards introduced the term amyloid degeneration for the conditions present, and this term has gradually passed into almost universal use. After the discovery of a practicable and easily applied test for the amyloid substance, it at once became easy to prosecute the search for this substance in the most varied organs, and to demonstrate the earliest traces of its occurrence. Now, also, the circle of diseased conditions, in the train of which amyloid degeneration of organs occurs, was rapidly enlarged; and finally it became possible to approach nearer to the question of the chemi-

cal nature of the substance under consideration, the solution of which question promises the most important conclusions respecting the true essence of amyloid disease. It therefore seems just to regard Virchow as the actual founder and greatest promoter of the doctrine of amyloid degeneration, as taught to-day. As regards the further progress which this doctrine has made since, we would refer to the studies of Kyber, cited above, where the history as well as the literature of the subject is given with satisfactory fulness.

So far as the amyloid liver, in particular, is concerned, its history cannot be separated from that of amyloid degeneration in general. The special studies which have been devoted to the amyloid liver have reference to the anatomical, and especially to the histological side of the question, which, indeed, has just lately been worked up more actively than ever, in consequence of the discovery of new reagents for amyloid matter (iodide of methylanilin, etc.). The pathology of amyloid liver, a very creditable description of which was given in Frerichs' classical work on diseases of the liver, has, it is true, received valuable contributions from the results of pathologico-anatomical, histological, and chemical investigations, and yet it has not, since the date of Frerichs' work, undergone any radical alterations. At the same time the pathology of amyloid liver still presents great hiatuses. The functional disturbances of the liver, in particular, as the result of this degeneration, have not yet been the subject of that thorough investigation which they deserve.

Amyloid degeneration of the liver consists in the fact that a substance foreign to the healthy organism, the so-called amyloid substance, is deposited in the parenchyma of the liver. The amyloid substance is a tolerably consistent, thick mucilaginous, colorless mass, of a peculiar waxy lustre, and almost of the transparency of glass. It is distinguished by its great resistance to all sorts of chemical influences, and especially also to decomposition. It is chemically characterized by its peculiar behavior

in the presence of iodine and sulphuric acid, a watery solution of iodine causing it to assume a mahogany-red color, which afterward, on the addition of sulphuric acid, changes to a blue or violet. This behavior, suggestive of that of starch (though the latter, it is true, is colored blue on the addition of iodine alone), gave occasion to the choice of the term amyloid for the substance under consideration. The same changes in color that appear on the application of iodine and sulphuric acid may also be produced in amyloid matter by using iodine and chloride of zinc, as well as iodine and chloride of calcium. Attention has lately been called to the fact that certain aniline colors, especially the iodide of methylanilin, will color amyloid matter of a bright ruby-red or violet-red, while tissues free from amyloid matter are thereby colored of a pale-blue.

Whereas at first the opinion was entertained that amyloid matter was closely related, in a chemical point of view, to the carbohydrates, evidence was furnished by Kekulé and C. Schmidt, as well as afterward by Kuehne and Rudneff, that amyloid matter was a nitrogenous body, belonging to the class of albuminoid substances. It is true, on the other hand, that it differs in various respects from substances of this class, especially in the fact of its insolubility in fluids containing pepsin.

The place of origin and method of origin of amyloid matter are even at the present day involved in entire obscurity. It may be looked upon as settled that amyloid matter arises from the albuminoid substances of the body; but, with regard to the more immediate method of this transformation, and particularly with regard to the place where it occurs, we know nothing. It is not determined whether amyloid matter is deposited in the tissues from without (from the blood), or whether it originates in the tissues themselves, at the points where it is found. Virchow, Rindfleisch, and others are of the opinion that the amyloid matter is brought to the tissues so affected by the blood—that is, by the transudation from the blood, and thus, so to speak, infiltrates those tissues. Rindfleisch considers it as most probable that the albuminoid substances of the nutritive fluid are arrested in their progress through the tissues, and are at once separated in a solid form. This view is favored by the fact that,

as a rule, the amyloid matter is first found in the walls of the smallest arteries and the capillaries of the diseased organs; but it is opposed by the fact that never, even in the highest grades of degeneration, has so much as a trace of amyloid matter been found in the blood. On the other hand, a number of circumstances favor the view that the amyloid matter originates at the points where it is found, within the tissues themselves; and, first, amyloid degeneration occurs, in extremely irregular distribution, in the vessels and parenchymal cells of the diseased organs. This seems to indicate that the parts concerned possess a varying degree of predisposition for degeneration, which would imply that the entire process is to be regarded as a local one, although dependent on general causes. But a second circumstance would appear to be of greater importance, viz., that, on careful application of the methylanilin test to the tissues infiltrated with amyloid material, certain changes in color are to be observed which seem to indicate that the foreign substance present in the variously colored portions may correspond to the various stages in the transformation of albumen into finished amyloid matter. Those shades of color point to the fact that a *gradual* transformation of albumen into amyloid matter takes place.

Amyloid degeneration of the liver never constitutes an independent isolated disease. For, aside from the circumstance that amyloid degeneration is always developed only in connection with certain chronic primary affections which profoundly disturb the general nutrition of the body, this degeneration of the liver is almost always associated with similar degeneration of the spleen, the kidneys, and other organs. In other words, the amyloid liver does not present itself as an independent, local malady, but merely constitutes a part of the general amyloid disease. The latter, however, is a disturbance of a progressive character, which, in the long run, does not confine itself to one single organ. We are not able to tell why amyloid degeneration attacks different organs sometimes in one and again in another order of consecution, why one or another organ sometimes remains free from the degeneration, and at other times is to the highest degree involved therein.

Etiology.

Amyloid degeneration of the liver, or of any other organ, is never observed as an independent, primary disease, but always has the significance of a secondary affection. For it arises only when the organism has suffered profound disturbances in its nutrition through a series of severe chronic ailments, and is thereby brought into a cachectic condition. Those primary affections which are liable to bring amyloid degeneration in their train, and which we may designate as the predisposing causes of amyloid disease, are, it is true, pretty well known to us. But, at the same time, we lack an insight into the actual connection between the rise of amyloid matter and the primary affections causing it, or rather the cachexia induced by these primary affections. We therefore have no knowledge of the *immediate* cause of amyloid disease.

Among the predisposing causes of amyloid liver, as well as of amyloid disease generally, may be enumerated:

1. *Prolonged suppuration and ulceration of bones and joints.*—This is most frequently caused by *caries* of one or more bones. The caries is developed by preference in children and youth as the result of cheesy or scrofulous ostitis of the spongy epiphyses of the long bones, as well as in the spongy portions of the short and thick bones, as of the vertebræ (psoas abscess), of the carpal and tarsal bones, etc. It may, furthermore, be caused by *necrosis* of bones. Necrosis of the long bones, the femur and tibia, with the development of open sinuses and the discharge of large quantities of pus, often gives occasion to the development of amyloid degeneration. We see the same result follow wounds of the bones when they give rise to tedious suppuration, as happens so often in compound comminuted fractures, but especially in gunshot fractures of the larger long bones. Chronic suppurations and ulcerations of joints, with destruction of the articular extremities and rupture of the capsule of the joint, in whatever way they may have been brought about and by whatever original disease they may have been caused, are very often followed by amyloid degeneration.

2. *Chronic suppuration and ulceration of soft parts* (with-

out implication of the bones), on the whole, much more rarely lead to amyloid degeneration than processes of this sort originating in the bones. Here it does not seem to make any particular difference whether the suppuration is on the surface or in the interior of the body. As a rule, however, the pus has an external means of escape, even though the suppurating surface may be internal. Among the primary affections that fall under this head, we may especially mention the chronic (so-called atonic or varicose) ulcers of the feet in elderly persons, as well as simple chronic ulcers of the skin generally, when they are extensive; likewise old fistulas—for instance, vesical, urethral, and rectal fistulas, and the like. Among the most frequent causes coming under this head is empyema of the thorax, whether a fistula into the pleural cavity exists or not. Furthermore, sacculated bronchiectasia with abundant secretion (in pulmonary cirrhosis), chronic abscesses (as hepatic abscess, or, more frequently, the abscesses from congestion associated with caries of the bones), purulent pyelitis and perinephritis, chronic dysentery, and other similar conditions have all been known to give occasion to amyloid disease. The same thing is accomplished now and then by the round gastric ulcer when it has attained an unusual size.

3. *Chronic pulmonary phthisis*, when accompanied by extensive ulceration and the formation of cavities within the lungs, very often leads to amyloid degeneration; and this is especially the case when there is at the same time widespread tubercular ulceration of the mucous membrane of the intestines, of the larynx, and of the trachea. In view of the enormous frequency of chronic pulmonary phthisis there is nothing surprising in the assertion that the absolute majority of all cases of amyloid degeneration of the liver, etc., may be traced back to the very conditions of disease just mentioned. Other forms of tuberculosis appear to be much more rarely followed by the same effects. Thus primary tuberculosis of the urino-genital apparatus, for instance, even when it has induced the most extensive caseous degeneration of the kidneys, the uterine mucous membrane, and other organs, but very exceptionally gives occasion to amyloid degeneration.

4. *Constitutional syphilis* likewise belongs to the more com-

mon diseases lying at the foundation of the degeneration in question, and has, from the beginning, been cited by observers as giving occasion to the same. Syphilis produces this result, especially in those cases which run their course with prolonged suppuration and ulceration of parts. Syphilitic bone-affections are most liable to be followed by amyloid degeneration, but syphilitic ulcerations of the skin and mucous membranes have the same result. At the same time amyloid degeneration is also seen to arise in the course of constitutional syphilis when no ulcerative processes have taken place either in bones or soft parts. Amyloid degeneration is associated with hereditary, that is, congenital syphilis, as well as with that acquired in later years, and, in fact, comparatively oftener with the former than with the latter. In congenital syphilis, according to the authority of Rokitansky and some others, amyloid degeneration of the liver is also said to occur as a congenital malady.

5. *Certain chronic constitutional diseases*, which seriously disturb the nutritive relations of the body and occasion general cachexia, give occasion, in individual instances, to the rise of amyloid degeneration. In this category may be placed long-continued intermittent fever, producing malarial cachexia, likewise mercurial cachexia, gout, rachitis, etc. With regard to some of these diseases doubts have been raised whether, in reality, they can, of themselves, bring about amyloid degeneration. So far as malarial cachexia is concerned, a condition which Rokitansky himself adduced as one of the causes of lardaceous liver, we may consider these doubts as set aside by observations more recently made. The mercurial cachexia, on the contrary, which has especially been blamed by English physicians as a cause of amyloid liver, and of which Frerichs said that its influence in the production of this degeneration was not sufficiently proven, is of late but rarely mentioned as the occasion of amyloid liver.

6. Finally, it is by no means so rare to see amyloid degeneration developed in the course of certain diseases associated with the formation of tumors, in connection with certain *neoplasms*. Tumors of the most various kinds, benignant as well as malignant, are sometimes followed by this degeneration. But they are only thus followed on condition that the neoplasm is slowly

developed, that it attains a considerable size, and especially on condition that the nutrition of the body is thereby lowered and a well-marked cachexia is produced. It is by no means necessary that retrograde metamorphosis, breaking down, and ulceration, should take place in the tumor, in order that amyloid degeneration be set up. The latter has been known to be associated with large ovarian tumors, of the cystic as well as the solid variety. I have seen amyloid disease of the liver arise in a man forty years of age, in whom an enormous fibro-myxoma had developed. This tumor, which originated in the cellular tissue in the region of the left kidney, and grew very slowly, finally reached a weight of thirty-eight pounds. Cancerous and sarcomatous tumors may also be followed by the same results, the more so the more slowly they are developed. Very malignant, rapidly growing neoplasms, which at an early period threaten life, do not allow time for the development of amyloid degeneration; but this is not true of the firmer cancers of the breast, the stomach, and the uterus, and particularly not of the colloid cancers, which usually run their course more slowly. When amyloid degeneration becomes associated with cancerous growths of the stomach, the uterus, etc., which are in a state of ichorous degeneration and of ulceration, the development of amyloid material seems to depend more on the loss of juices incident to the ulceration than on the neoplasm itself, that is, on any considerable size of the latter. Amyloid degeneration has also been known to be associated with leucæmia, and still more frequently with pseudo-leucæmia.

In quite rare instances amyloid degeneration of the liver and of other organs is observed without our being able to attribute it to any of the above-mentioned primary affections, or to anything like them as a cause. Wilks already cited such cases (loc. cit.) under the name of "simple lardaceous disease," and more recent observers confirm the fact by further examples of the kind. It does not, however, seem permissible, with all our experience concerning the nature of amyloid degeneration, to regard such cases as *primary* amyloid degeneration, as has been done by some. For even in these instances the amyloid degeneration is always associated with general cachexia, which must, after all, in every

instance have some definite cause, even though this is not always apparent to our eyes.

With regard to the comparative frequency of the coincidence of amyloid disease with the several classes of the above-named primary affections, we have, it is true, certain individual statistical statements before us; but the first glance at the figures given shows that they are not the expression of the actually existing average relationship between them, but that accidental circumstances have influenced the results reached. The great differences in the statements of different observers on this subject are simply referable to the fact that the hospitals from which these statements emanate draw their inmates from different groups of the population, and that accordingly the primary affections with which amyloid degeneration eventually becomes associated are represented with varied frequency in the several institutions. Thus Hoffmann found among 80 cases of amyloid disease only 6 (7.5 per cent.) which were caused by chronic suppuration of bones, while O. Weber refers not less than 14 out of 37 cases (38 per cent.), and E. Wagner 11 out of 48 cases (23 per cent.), to this primary affection. The same differences are found with regard to other diseased conditions leading to amyloid degeneration. Only this much may be considered as settled, viz., that, as we have already stated, the absolute majority of cases of amyloid disease are to be referred to chronic pulmonary phthisis. Hoffmann counted 54 such among his 80 cases, equal to 67.5 per cent.; O. Weber 15 among his 37 cases, equal to 40.5 per cent.; E. Wagner 27 among his 48 cases, equal to 56.25 per cent.

So far as the occurrence of amyloid liver at the various periods of life is concerned, it may, indeed, be observed at all ages, but with very varying degrees of frequency. According to the evidence of Rokitansky and others, amyloid liver even occurs as a congenital condition — for instance, in hereditary syphilis. But it may likewise be met with in old age. If we remember the nature of the primary affections with which amyloid disease is associated, and the period of life at which those affections are most prone to exist, we shall readily understand the fact, confirmed by general experience, that amyloid liver occurs most frequently between the ages of ten and thirty.

Frerichs found, among 68 cases:		Wagner found, among 48 cases:	
Under 10 years of age	3	Under 10 years of age	5
Between 10 and 20	19	Between 10 and 20	5
" 20 and 30	19	" 20 and 30	18
" 30 and 50	18	" 30 and 50	13
" 50 and 70	9	" 50 and 70	7

Even in these figures we may observe the varied combination of the material for observation in the hospitals concerned. Amyloid liver occurs considerably more often in the male than in the female sex. Of Frerichs' 68 cases, 53 were men and 15 women; of Wagner's 48 cases, 33 were men and 15 women. Frerichs justly remarks with regard to this circumstance, which is likewise confirmed by universal experience, that this difference in the frequency of amyloid liver in the two sexes is the more striking because the diseases which induce this degeneration by no means especially affect the male sex.

Pathological Anatomy.

When amyloid degeneration occurs in its pure form, and has reached a very high grade, the liver shows exceedingly characteristic alterations. The organ is enlarged to a variable degree, sometimes quite enormously, and indeed this enlargement involves all three dimensions and all divisions of the liver quite uniformly. The liver of an adult in some instances reaches a weight of twelve pounds, and even more. I have seen the liver of a child ten years old but little below this weight. On an average the liver attains perhaps twice its normal weight. The serous covering of the liver undergoes no change through amyloid degeneration; it remains smooth, transparent, and tense, and does not become adherent to neighboring parts. The anterior sharp edge of the liver appears thickened, somewhat bevelled, or even with a quite thickly rounded border. Still, this change of form is by no means so constant as might be expected from the statements of some authors, for even in the higher grades of degeneration the edge in question may retain its sharpness almost unchanged. Even in its external appearance the amyloid liver appears very poor in blood; its color is a peculiar light grayish

brown or yellowish gray, sometimes with an admixture of red. The consistency of an amyloid liver is very striking. It seems very resisting to the touch, of an almost rubber-like firmness. Harder pressure with the finger, as in the case of compact œdema, makes an impression which disappears but slowly and imperfectly. Its consistency is therefore of a firm, doughy character. A certain contrast to this increased resistance to pressure is furnished by the comparative ease with which the amyloid liver can be cut. Although it is somewhat harder to cut than the normal liver, still the knife by no means encounters the resistance which one might have expected from the mere touch. The first thing to be noticed on the cut surface is the remarkably high degree of anæmia. Only the coarser vessels give escape to a certain amount of thin blood or serum; otherwise the tissue seems dry, almost bloodless, of a very pale, grayish yellow, or dirty, grayish brown color, sometimes with a reddish glimmer through it, similar to a strongly-smoked ham. The cut surface never appears entirely homogeneous; even in the highest grades of degeneration the acinous structure is still indicated, the lobules of the liver being separated from one another by a fine, pale yellow, opaque line. A similar opaque, pale spot likewise appears in the centre of each lobule. On section, the tissue of the amyloid liver presents a characteristic dull, waxy lustre. Others prefer to compare the appearance of the cut surface to that of lard. In addition to this lustre, the amyloid liver is distinguished by the peculiar transparency of its tissue; thin sections of the same held against the light show an almost glassy transparency which is only interrupted by the opaque boundary lines of the lobules and their central points. On the addition of a watery solution of iodine, the glassy portions—that is, the portions which have undergone amyloid degeneration—assume a lively reddish brown hue, while the opaque lines and points are merely colored of a pale yellow. Another noticeable peculiarity is the fact that the amyloid liver, as well as other amyloid parts, long resist decomposition, although this is a piece of evidence the development of which one will hardly care to await.

In cases where the amyloid degeneration has attained but a low grade, or where other alterations in the tissue of the liver

exist, the picture presented by amyloid liver is essentially different. Enlargement and increased weight of the organ are not always to be found where the degeneration has progressed far enough to be plainly demonstrable by the eye, without the aid of chemical reagents. The rounding-off of the otherwise sharp anterior border of the liver may, under these circumstances, also be missed. But, corresponding to the degree of degeneration present, the organ will always show, in a more or less marked manner, a certain increased consistency to the touch, an unusual degree of bloodlessness, the pale, grayish yellow color, the waxy lustre of its cut surface, and the transparency of the tissue infiltrated with amyloid matter. In the slighter grades of amyloid liver the cut surface, on close inspection, shows certain deviations from the picture given above. The glassy transparency and the peculiar pale-gray color do not extend over the entire hepatic lobule, but only appear in certain isolated little points or in certain zones of the lobule. The marginal portions of the lobule, as well as its centre, consist of the original liver-tissue, while between the two is situated a variably wide zone, transparent in quality and of a pale-gray color. Amyloid infiltration, therefore, as was very well set forth by Rindfleisch, arises first in the middle zone of each lobule (in the region designated by Rindfleisch as the area of inosculation of hepatic arterioles), and extends from there toward the centre, and finally toward the periphery of the lobules.

The slightest grades of amyloid liver are not to be recognized by the naked eye, but require microscopic examination, with the simultaneous aid of the iodine and sulphuric acid, or some similar test. Care must, however, be taken that the specimens to be examined be first thoroughly freed of blood; otherwise, errors are possible. If we proceed correctly and methodically, however (especially if we use thin sections hardened in alcohol, and not the fresh liver-substance), we shall be able in this way, not only readily to determine the presence or absence of amyloid matter in doubtful cases, but also to obtain a very accurate insight into the degree and the extent of the degeneration.

It often happens that the amyloid degeneration does not extend uniformly over the entire liver, but leaves certain por-

tions thereof quite free, and shows itself in other portions only in its first beginnings, while in still other portions it involves the half, or even the whole, of each lobule. These various stages of degeneration show themselves distributed in an irregular manner on the cut surface, sometimes being gradually merged into one another, and sometimes being pretty sharply separated. In quite rare instances amyloid degeneration of the liver appears not generally diffused, but as a deposit of amyloid matter about certain foci, in the shape of lardaceous nodules not sharply outlined, while the main mass of the liver is quite free from this material. A case of this kind is reported by Rindfleisch (loc. cit.). Perhaps Rokitansky had something similar in mind when he mentioned the occurrence of whitish, lardy nodules in the liver.[1] Still it is possible that he may have referred to syphilitic nodules in the interior of the amyloid liver.

The deposit of amyloid matter in the liver may also occur when the organ is already the seat of other morbid changes; and, *vice versâ*, other changes may be added to an already existing amyloid liver. Thus complex conditions arise with regard to which we cannot always say in what order of time the individual disturbances have been developed, nor in what relation they stand to one another.

The amyloid liver is quite commonly, at the same time, a fatty liver, and sometimes the one, sometimes the other metamorphosis is in the ascendancy as regards the amount of space occupied. As a rule, we shall then find the marginal portions of each lobule infiltrated with fatty matter—hence opaque and of a whitish yellow color; while the remainder of the lobule is infiltrated with amyloid matter—hence transparent and of a light-gray color. This combined degeneration is also frequently not uniformly distributed over the entire liver, the fatty degeneration being in the ascendancy in one portion, while the amyloid degeneration prevails in another. There can be no doubt that, as a rule, the liver was already the seat of fatty infiltration (generally as the result of antecedent wasting diseases) when the deposit of amyloid matter began. But in some instances the

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[1] Handbuch d. pathol. Anat. 1842. III., p. 311.

fatty infiltration of the marginal portion of the lobules may be regarded as the result of the amyloid degeneration, inasmuch as, after the destruction of numerous liver-cells by this degeneration, the remaining supply of cells is not sufficient properly to dispose of the material brought to them, a portion of which therefore accumulates within the cells in the form of fat. The amyloid fatty liver may present itself in the form of a very voluminous tumor; still, such livers are by no means always notably enlarged.

The other possible complications of amyloid liver are of but slight significance. The deposit of amyloid matter may take place in the cirrhotic liver, the lobulated syphilitic liver, or in livers disseminated with syphilitic nodules in the most varied stages of development. The latter complication in particular is comparatively frequent. Metastatic abscesses may be developed in the amyloid liver, which are worthy of notice from the fact that we may see amyloid matter floating about in them in the form of large flakes. Tumors also sometimes arise in the amyloid liver. They interest us, inasmuch as they imply the fact of prompt absorption of amyloid matter. In a man, twenty-eight years of age, the victim of lymphatic pseudo-leucæmia, I recently saw an amyloid liver of the purest form, in the interior of which there was developed a lympho-sarcomatous tumor of about the size of a goose-egg, as well as several smaller nodules. In this case the circumstances placed it beyond a doubt that the tumors were of much more recent date than the amyloid degeneration, that consequently the tissue when in a state of the highest amyloid infiltration must have been absorbed in order to make place for the neoplasm. Microscopic examination showed that there was no trace of amyloid matter within the area of the tumors, even the finer blood-vessels in the same were entirely free from this substance.

With regard to the condition of the *bile* in amyloid liver, one would expect that the disease of the liver would show itself in this fluid likewise. This is, however, by no means always the case. Even in the highest grades of amyloid liver we often enough find the gall-bladder filled with a moderate amount of normal looking bile. Sometimes there is even highly inspissated black-

ish-green, thick, mucilaginous bile to be found in the gall-bladder (after the bile has been long retained there). In other cases, however — and this only in those that are most pronounced — the gall-bladder contains a thin, mucilaginous, almost colorless, or pale yellowish, clear fluid, in moderate amount; and chemical examination has, in some cases, shown that this fluid contains mere traces, not only of biliary coloring matter, but also of biliary acids; that, consequently, this fluid is not actually bile, but merely the diluted product of secretion of the mucous membrane of the biliary passages (Hoppe-Seyler).

So far as other anatomico-pathological conditions in amyloid liver are concerned, the dead body is almost always greatly emaciated, extremely anæmic, and generally also dropsical. It is quite exceptional for the bodies of such subjects to be tolerably well nourished, the subcutaneous cellular tissue being comparatively rich in fat. In such cases, then, the cachexia upon the basis of which the amyloid liver was developed has again been recovered from. Almost invariably the primary disease which has given rise to the amyloid degeneration is still in full progress, or has, at least, left unmistakable anatomico-pathological alterations behind it. Aside from the amyloid liver, the spleen, the kidneys, the intestines, and other organs are very often infiltrated with amyloid matter. In the severer cases of amyloid liver there is generally ascites and œdematous swelling of the lower half of the body.

The most important question in connection with amyloid liver undoubtedly is: in what tissues is the amyloid matter deposited, and what relations do the individual tissue elements of the liver bear to this degeneration? Is it the secretory cells of the liver, is it the blood-vessels of the liver, and if so, which ones, or is it the connective tissue of the organ in which the amyloid matter accumulates? These questions, which of course cannot be determined otherwise than by microscopic examinations, have from the beginning actively engaged those who have especially studied the amyloid liver. Singularly enough, this apparently

simple question is, however, not yet definitely settled; indeed, the views on this subject, even at the present day, are tolerably antagonistic to each other. The point which is most in dispute is the part taken by the liver-cells in the amyloid infiltration. On the one hand it is asserted that the liver-cells alone take up the amyloid matter; on the other hand, that they never do this, and that it is exclusively the walls of the capillaries which are infiltrated with this matter, the liver-cells perishing by atrophy from pressure. A third party, again, claim that the liver-cells, as well as the capillaries lying between them, fall into amyloid degeneration; and, finally, the opinion has recently been advanced that it is neither the glandular cells nor the blood-vessels, but the connective-tissue sheaths of the latter, that take up the amyloid matter. Under these circumstances it seems fitting to introduce briefly the views of some of those authors with regard to whom we may take it for granted that they have independently tested the subject of the course of the degeneration and the part taken therein by the different tissues.

Rokitansky, and likewise H. Meckel, merely emphasize the degeneration of the liver-cells, and leave the blood-vessels entirely out of the account.

Virchow[1] teaches that amyloid degeneration generally begins in the smallest arteries. Not until the transformation of their walls has reached a high grade can the infiltration extend to the surrounding parenchyma. But this does not often happen. More frequently the parenchyma atrophies, and the disease extends to the capillaries, which then swell up and press the liver-cells to death. As the finest branches of the hepatic artery are always first attacked, the middle zone of the lobules is always the first to suffer, that being the part where the branches of the hepatic artery break up into capillaries and anastomose with the capillaries of the portal vein. If the process also extends to the capillaries, these likewise swell up and become friable; in fact, the disease may even attack the intra-lobular veins, whereas the inter-lobular vessels are but very rarely involved. If the liver-cells themselves are implicated, we may see the contents of the

[1] Cellularpathologie, 3. Aufl. S. 334.

same become at first slightly turbid and then quite homogeneous, the muscles and the membrane of the cell disappear, and a shining, homogeneous mass remain. In this way all the cells of the zone in question may perish, and in very high grades of the disease the entire lobule may become amyloid.

Frerichs[1] describes the relation of things less clearly and positively. According to him, the amyloid degeneration begins in the glandular cells or in the finest branches of the hepatic artery, and gradually spreads from the middle of the lobule over its entire extent. The branches of the hepatic artery are preeminently attacked, but the process likewise extends to the capillaries and to the beginnings of the veins.

In opposition to these views, E. Wagner (loc. cit.) made the assertion, as early as the year 1861, that amyloid degeneration of the liver was always confined to the finer blood-vessels of the same, and that the liver-cells themselves were never found infiltrated with amyloid matter. The capillaries of the lobule swell up by the reception of amyloid matter into their walls, and exert a pressure on the liver-cells, the greater part of which are thereby thrown into a state of atrophy and entirely disappear. So far as the liver-cells are preserved, they appear turbid and filled with fat-drops, especially at the margin of the lobule.

For a long time Wagner stood entirely alone in this opinion. The majority of the observers who immediately followed him held essentially to the views which Virchow had given of the matter; they admitted the part which the blood-vessels take in the degeneration, but also held to the opinion that the liver-cells were at the same time found infiltrated with amyloid matter to a greater or less degree. To this class of authors belong Foerster, Billroth, Friedreich, and others. Some even give marked prominence to the amyloid degeneration of the liver-cells, as, for instance, B. Rindfleisch and Klebs.

Rindfleisch indeed admits that the branches of the hepatic artery first of all show amyloid degeneration, and that in every lobule the degeneration first arises at the point where these arterial branches open into the portal capillary system, therefore

[1] Loc. cit., p. 167 et seq.

half way between the margin and centre of the lobule. In his opinion, however, the degeneration extends not from the arterioles to the capillaries, but to the liver-cells, which swell up into roundish flakes, several of which unite to form a shining, cylindrical mass. The degeneration advances from the liver-cells of the middle zone of the lobule toward its centre, therefore into the domain of the hepatic vein, and only later and in higher grades of degeneration does it also extend to the cells in the domain of the portal vein, that is, the marginal zone of the lobule.

According to Klebs,[1] the degeneration may, it is true, be confined to the arteries and capillaries, but in such cases it can only be demonstrated by chemical tests. But whenever amyloid degeneration can be discovered macroscopically, by the outward appearance and the altered consistency, then it is claimed that the liver-cells are always likewise involved.

Among the authors who have quite recently occupied themselves with the question under consideration, Cornil (loc. cit.), on the occasion of trying the iodide of methylanilin test, declares that he saw the liver-cells remain free from amyloid matter, and that the walls of the capillaries alone take it up. Still, in view of the authorities that have advocated the participation of the liver-cells in the infiltration, and in view of the small number of amyloid livers examined by him, Cornil does not look upon the question as being settled by his observations.

The above-named position of E. Wagner has been most nearly approached by Tiessen, Heschl, and Schuette, or Schuette's teacher, Koester. Tiessen claims to prove that the liver-cells never take up the amyloid matter. The amyloid masses stand rather in the closest relations, as regards space, to the capillary walls, while the liver-cells are crowded to death by those masses and fall victims to atrophy. But Tiessen does not admit that the true capillary wall, that is, the tube of endothelial cells itself, is infiltrated, but he regards the amyloid matter as an amorphous secretion which accumulates externally around the uninjured capillary wall. Tiessen leaves it unsettled whether

[1] Handbuch d. pathol. Anatomie. I., p. 408.

the amyloid flakes are deposited in previously formed cavities (the only cavities that could be meant are doubtless the perivascular lymph-spaces believed in by Biesiadecki), or whether they push themselves in between the capillaries and liver-cells, after having broken down the loose connection between the two structures. Tiessen is not ready to declare himself in favor of the theory—which is, however, permissible—that the amyloid mass may be infiltrated into the delicate connective tissue constituting the *adventitia capillaris* of the hepatic capillaries.

Finally, Heschl's views still remain to be presented. This observer likewise establishes it as a fact that the liver-cells themselves never fall into amyloid degeneration, but that they merely disappear under the pressure of the amyloid masses. Heschl coincides in so far with Tiessen as to hold that the amyloid matter is a deposit between the capillary walls and the liver-cells; he accordingly designates the amyloid liver as an interstitial infiltration of this organ. But he does not express himself positively as to whether he believes this infiltration to be combined, at the same time, with an amyloid transformation of the perivascular connective tissue of the hepatic lobules.

The opinion of Schuette coincides almost point for point with that of Tiessen, which is the more worthy of notice, as it was published at about the same time with that of Tiessen, both authors having, to all appearances, worked entirely independently of each other. At all events, neither of them mentions the name of the other.

According to my own observations on the course of amyloid degeneration of the liver, I am led to coincide with the views of E. Wagner, as already announced. I believe I have thoroughly satisfied myself that infiltration of the liver-cells with amyloid matter never takes place, but that the only parts thus affected are the blood-vessels; that, aside from the minute branches of the hepatic artery, the entire capillary system of the lobule is affected, the small veins being also involved toward the last, and to a lesser degree.

For microscopic examination it is best not to employ fresh portions of liver, but only those which have been hardened in alcohol. The examination is greatly facilitated by the simultaneous use of a solution of iodide of potassium, or the

newly recommended iodide of methylanilin, the latter in the form of the Dresden parlor-ink of Leonhardi, a few drops of which added to a watch-crystalful of distilled water is sufficient, in the course of a few minutes, to give a ruby-red color to the amyloid portions, while the non-amyloid tissue retains a pale blue, cloudy appearance. In the branches of the hepatic artery amyloid degeneration shows itself in the fact that the walls of the same grow thicker, swollen, of a glassy lustre, and highly transparent, and that the structure of their walls entirely disappears, the latter assuming, therefore, a homogeneous appearance. The calibre of the small arteries appears to be but little narrowed thereby. The capillaries, on the contrary, by taking up the amyloid matter, are transformed into shining, transparent, and, at the same time, entirely homogeneous tubes, which are considerably thicker than the normal capillaries (two to three times as thick). The swollen, enormously thickened capillary walls leave but a very narrow calibre to the vessels, and, on the other hand, press against the surrounding liver-cells, causing atrophy, and soon the entire disappearance of the latter. The degeneration in the capillaries begins in such a way that, on transverse section of the same, one sees shining, semilunar, or sickle-shaped swellings, but on a longitudinal section spindle-shaped or club-shaped swellings which change their form into a band of uniform width corresponding to the thickness of the swollen capillary wall. In higher grades of the disease the capillaries are always uniformly affected; they are equally thick at every portion of their walls; in milder grades the swelling only extends to a portion, perhaps only to half of the transverse section of the capillary. Some circumstances, indeed, appear to me to argue in favor of the view held by Heschl, Tiessen, and Schuette to the effect that, while the amyloid matter does follow in close contact to the walls of the capillaries, the cell-tube which constitutes the actual capillary wall remains unaltered, and is only enclosed by the amyloid matter as by a sheath. But we will not here dwell any further on this point. So far as concerns the course of amyloid degeneration in the liver, the branches of the hepatic artery are first attacked, then it extends to the capillaries of the lobules in such manner as rapidly to attain a high grade in the middle zone of each lobule, while in the marginal portions of the same at first but a few single transverse sections of capillaries appear swollen and amyloid. While, then, the condition of the marginal zone remains the same for the present, the degeneration as a whole advances from the intermediate zone toward the central vein, and when it has come quite near to the latter it finally also extends to the periphery of the lobule. In the highest grades of degeneration but a narrow strip of liver-cells, chiefly in a state of fatty infiltration, can still be seen at the outermost margin of the hepatic lobule, and in the same way a few generally quite atrophied liver-cells may be encountered in the immediate vicinity of the central vein. All the remainder of the parenchyma has perished, but the biliary passages and their epithelium remain, under all circumstances, quite intact.

Pathology.

It is difficult to determine what influence amyloid degeneration exerts on the functions of the liver, and how far the disturbed liver-function again reacts upon the general organism. We must remember that in amyloid liver we are dealing not merely with a local evil, but with a profound disturbance of the processes of nutrition of the entire organism, and that this does not arise primarily, but joins itself to prolonged, exhausting processes of disease, which themselves already carry with them the most varied evil consequences to the body. It is therefore difficult to determine the share of responsibility which, in each individual case, is to be charged to the account of the amyloid liver.

The most important result of amyloid degeneration is the destruction of the liver-cells. Even if those men should be right who believe that the liver-cells themselves take up the amyloid matter, still, so far as their function is concerned, this would mean the same as destruction of the cells. For we cannot possibly admit that amyloid flakes, or a cell-body permeated and distended with amyloid matter, which has lost all the characteristics of a cell, should still be able to take part in the functions of the organ. But the few liver-cells which remain are to a great degree in a state of simple or fatty atrophy—that is, of fatty infiltration. We must, therefore, at all events take it for granted that there is a great diminution of function in the amyloid liver. To this is added the disease of the capillaries, which we cannot conceive of without associating it with changes in transudation, and therefore in the nutrition of the tissues. It is true that we are not in possession of any further particulars on this last point. The extraordinary poverty in blood of the amyloid liver might be of still more weight in causing the disturbance of its functions. Here, again, we are unable to determine how far this poverty in blood depends on the amyloid infiltration of the hepatic capillaries, and how far it depends on the general anæmia. The amyloid degeneration of the capillaries is, to all appearances, associated with a considerable narrowing of the same. Perhaps we over-estimate the degree of this narrowing; at all events, it is certain that even highly degenerated livers can be injected with-

out any special difficulty. But at the same time the poverty in blood of the amyloid liver is so enormous, and so much greater than that of other organs in the same body, that we must, in part at least, regard it as being in a causal connection with the disease of the capillaries.

The conditions under which the functions of the amyloid liver are lost are, on the one hand, a high grade of anæmia of the liver, a hydræmic condition of the entire mass of the blood, and a lack of blood corpuscles; on the other hand, the destruction of most of the liver-cells, and other kinds of degeneration of a part of the remaining parenchyma. So far as the formation of glycogen and then of sugar is concerned, we may at once accept the fact that this is diminished to a degree corresponding to the destruction of liver-cells. In some cases [1] this has been positively demonstrated. The secretion of bile seems not always to be reduced to the extent that one would suppose, judging by the grade of the liver degeneration. In the worst cases, however, the secretion of bile is reduced almost to nothing, the gall-bladder containing a colorless, clear, thinly mucilaginous fluid, which merely shows traces of biliary acids (Hoppe-Seyler).

General Picture of the Disease.

Persons affected with amyloid liver, with but quite rare exceptions, present the picture of a high grade of general cachexia. They are emaciated, poor in blood, of a pale complexion, and inclined to dropsical exudations. The picture of the disease naturally varies in individual cases, according to the nature of the disease which has given occasion to the amyloid liver, as well as according to the extension of the degeneration to the spleen, the kidneys, and other organs. But the cachexia, which was already more or less developed before the beginning of the liver-swelling, stands forth all the more prominently, and makes all the faster progress as soon as the amyloid tumor of the liver is added thereto. The picture of the disease undergoes no striking change during the further progress of the malady. The general

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[1] *Frerichs*, Klinik der Leberkrankheiten. II., p. 171.

condition grows gradually worse, while the swelling of the liver gradually increases, until finally œdema of the lower half of the body and ascites, or even general dropsy, sets in, and the patient dies with all the signs of extreme exhaustion. Under appropriate treatment, the increase in size of the liver may, it is true, be for a time arrested, and even a reduction in its size be observed, but it is very doubtful whether this implies a recession of the amyloid infiltration. Such temporary fluctuations in the course of the disease are not capable of averting the fatal termination.

Symptomatology.

The decisive symptom of amyloid liver is the enlargement of the organ which is present in the vast majority of instances, and which, at all events, will not be missed if the degeneration has attained a high grade. The increase in size of the liver varies within tolerably wide limits; as a rule, however, it reaches about double its normal dimensions. The weight of the organ may be from six to eight pounds, in some instances even from ten to twelve pounds. If the degeneration is only beginning, the liver is normal in size, or at least not noticeably enlarged; indeed, in some cases the degeneration is found to have advanced tolerably far, in spite of the normal size of the organ. Under some circumstances the amyloid liver is even diminished in size, viz., when the degeneration in question has been preceded by other processes which lead to shrinking of the organ (as syphilis, cirrhosis). Very large amyloid livers extend a hand's breadth or more below the margin of the ribs, crowd the diaphragm upward, and widen the lower part of the bony walls of the thorax, as the liver does not find the requisite room in the hypochondrium. The liver, advancing below the lower margin of the ribs, can be felt through the abdominal walls as an extremely resisting tumor of almost wooden hardness. Its anterior margin can be grasped, provided the abdominal walls are not too tightly stretched (by ascites, for instance, or by tumors in the abdomen), and we may then recognize the fact that this margin has lost its sharpness, and has been, to a certain degree, rounded off. In greatly ema-

ciated patients with very large amyloid livers, and especially in children, one may even be able, by the eye, to determine the position and the lower boundary of the liver tumor.

The amyloid liver feels perfectly smooth to the hand of the examiner, provided no other processes of disease have altered the surface of the organ. Aside from a certain sensation of fulness and pressure in the hypochondrium and the region of the stomach, the patient experiences no abnormal sensation from his enlarged liver. Even tolerably hard pressure on the liver is borne without any special increase of that sensation. It is only when more tense adhesions of the liver to neighboring organs have taken place, and especially when there is diffuse peri-hepatitis with universal adhesion of the liver, as may occur in cases dependent on syphilis, that the patient complains of lively, piercing pains in the region of the liver.

Disturbances in the escape of bile do not occur in amyloid liver; this disease of itself, in particular, never leading to the retention of bile and to icterus. If icterus arises in the course of amyloid liver, which seldom enough happens, the cause thereof lies in circumstances which stand in no direct connection with the liver degeneration; for instance, in the pressure which enlarged portal lymphatic glands exercise on the larger biliary passages.

One would suppose that the amyloid degeneration of the capillaries, especially on account of the consequent narrowing of the same, would cause serious obstruction to the passage of the portal blood through the liver, and would thus lead to stagnation in the domain of the portal vein. But disturbances of this kind, as a rule, are not prominent in amyloid liver. It is true that the higher grades of this degeneration are liable to be associated with ascites. But in the absence of other signs of obstruction of the portal circulation, the ascites might more readily be referred to the hydræmic constitution of the blood than to hindrances of the circulation within the liver. Often enough, even in advanced liver-degeneration, there is no ascites as well as no other sign of any difficulty in the circulation through the liver.

Amyloid liver is very frequently accompanied by a *tumor of*

the spleen, which generally also depends on amyloid degeneration. According to the variety of primary affection which the amyloid disease has followed, the enlarged spleen will likewise have the character of a swelling dependent on syphilis, on intermittent, on leucæmia, or pseudo-leucæmia. No definite clue to this is furnished either by the size or by the consistency and characteristics of the surface of the tumor, for all the tumors named feel firm and smooth. But an enlarged spleen is by no means always an accompaniment of amyloid liver, for neither does degeneration of the spleen always take place with that of the liver, nor is the amyloid spleen always distinctly enlarged. An enlarged spleen is encountered in somewhat more than half of all cases of amyloid liver, and in about two-thirds of these cases the tumor of the spleen is amyloid in character.

In amyloid liver there is often no symptom whatever referable to the stomach and intestinal canal. The thing most likely to make itself felt is the diminished production of bile. The stools are then very pale, gray, sometimes quite colorless, while at other times they are again more actively colored. The absence of bile in the intestinal canal causes abnormal processes of decomposition in the contents of the intestine, with an abundant development of gases, causing tympanites of the intestines, and the escape of fetid wind.

In some cases of amyloid liver, however, the disturbances of the stomach and intestines make themselves prominent. The appetite is lost; from time to time vomiting sets in. But the most important manifestation is the diarrhœa, whereby masses of a pale color and mucilaginous quality are evacuated. These attacks of diarrhœa set in without any definite external cause, are very obstinate, often last for weeks or recur from time to time at short intervals. The cause of the diarrhœa lies in anatomical lesions of the intestinal mucous membrane. This is either the seat of amyloid degeneration or of ulcers of various kinds, most frequently tubercular ulcers. Still, in such cases, the diarrhœa may also be caused by syphilitic or simple follicular ulcers, or by leucæmic and pseudo-leucæmic infiltration of the mucous membrane. Naturally, the profuse secretion from the bowels, as well as the disturbances of digestion and absorption, cause a

material aggravation of the already existing anæmia and more rapid progress of the emaciation.

The secretion of urine is not in itself strikingly altered in amyloid liver. In so far, however, as the degeneration of the liver very often goes hand in hand with that of the kidneys, there is then a secretion of albuminous urine. Albuminuria is present in the majority of cases of amyloid liver.

Finally, dropsy still remains to be considered as a symptom of amyloid liver. Dropsical transudations may be found in the majority of cases, especially during the later stages of the disease, though they are certainly lacking in some cases at all times. Sometimes the lower extremities alone are œdematous and swollen, sometimes the œdema extends over the whole body. As already stated, there is generally ascites present also, but this does not attain any considerable degree. All these circumstances render it probable, as Bamberger has shown in opposition to Budd, that the dropsy is to be referred to the hydræmic condition of the blood, and not directly to the amyloid liver.

Aside from the cachexia, the anæmia, and the dropsy, no other general symptoms belong to amyloid liver. Fever, in particular, is not liable to exist, and when it does it has nothing to do with the amyloid liver, but is called forth by other accidental processes of disease, or it belongs to the primary affection, in the wake of which the amyloid degeneration has arisen.

Diagnosis.

The local manifestations on the part of the liver must be designated as the leading symptoms for the diagnosis of amyloid liver. The demonstration of a distinctly or even very greatly enlarged liver, the enlargement being uniform in all directions, which shows quite uncommonly firm resistance to the touch, sometimes feeling as hard as a board, but which has a smooth surface, and is not sensitive on pressure, and which has, furthermore, increased in size quite gradually, argues in favor of an amyloid liver. If we meet with such a liver-tumor in a cachectic individual who has suffered from caries and necrosis, from chronic suppuration of any kind, or who shows signs of syphilis,

of pulmonary consumption, or of any of those diseases which we have cited as lying at the foundation of amyloid degeneration, then there can be scarcely a doubt about the diagnosis of amyloid liver. It becomes all the more certain if, at the same time, there is a firm and smooth spleen-tumor present, and if the urine contains albumen; if, therefore, there are signs of amyloid degeneration of the spleen and kidneys. The enlarged liver, however, cannot always be safely judged of by its consistency; it is possible to confound it with hyperæmic swellings, with hypertrophy of the liver, with the leucæmic liver-tumor, and, above all things, with the fatty liver. Here we must proceed by means of exclusion. We are not justified in looking for hyperæmic swellings of the liver in extremely anæmic and cachectic individuals; we may guard against error in the matter of leucæmic tumors by an examination of the blood, by the tendency to hemorrhages that exists in leucæmia, etc. It is most easy to imagine a mistake being made as between amyloid liver and fatty liver, because the latter comes nearest to the former in size and smoothness, and is often developed under the same circumstances; that is, in the train of various wasting diseases which are also followed by amyloid degeneration. If, however, a simple fatty liver is present (not the lardaceous fatty liver), this will betray itself by its much softer consistency; the enlarged spleen and the albuminuria are also more likely to be wanting, and, finally, the fatty liver by no means takes as deep a hold on the general processes of nutrition as does the amyloid liver.

In some instances the diagnosis of amyloid liver cannot be made with certainty; we can at best, with more or less good reason, conjecture the disease to be present. The diagnosis is impossible if the liver is not enlarged, for then its consistency can also not be determined. At the same time, in spite of the failure of any increase in size, a mild grade of amyloid liver may be presumed to exist when one of the diseases leading to amyloid degeneration is present, when cachexia and anæmia are highly developed, and when, in addition to a smooth and firm tumor of the spleen, albuminuria can be demonstrated.

Duration, Terminations, Prognosis.

Amyloid liver always pursues a very tedious course, unless the latter is cut short by some intercurrent accident not directly connected with the liver-degeneration. The disease always extends over a series of months; but its duration cannot be quite positively determined, because the beginnings of amyloid degeneration entirely elude our notice.

It was formerly believed that the primary affection which, in any given case, gave occasion to the amyloid degeneration, must have existed for a very long time, if possible for years, before the degeneration in question could be developed. We now know, from the communications of Cohnheim,[1] and other experiences, that at least in suppurations of bones (after gun-shot wounds, etc.) a period of about three months is sufficient to bring about amyloid degeneration.

When the disease has once begun, however, its further progress, as a rule, is very uniform; there are no interruptions or retardations, no exacerbations of the process, nor can any special stages be distinguished in its course. The condition grows very gradually worse, until finally death takes place, caused by general exhaustion. It cannot be determined how much of this condition of extreme exhaustion is to be attributed to the amyloid liver, and how much to the simultaneous degeneration of the spleen and kidneys or to the primary diseased processes. Sometimes the patient does not die outright of exhaustion, but of some intercurrent disease, or of some one of the sequels of the primary affection that happens to underlie the amyloid disease; as, for instance, of pneumonia, peritonitis, œdema of the lungs, etc.

The continuance, during the progressive development of amyloid liver, of the diseased processes causing the amyloid degeneration, makes it almost impossible, aside from other circumstances, to say whether the cure of amyloid liver takes place or not. Excellent physicians (Frerichs, Graves, Budd, and others)

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[1] Virchow's Archiv. LIV., p. 271.

are of the opinion that more recent infiltrations, under some circumstances, recede, and in evidence thereof adduce instances in which even very considerable intumescences of the liver have grown smaller under appropriate treatment. But, inasmuch as the diagnosis of amyloid liver is generally uncertain, as long as the case is still recent and not too far advanced, it is easy to understand why doubts should ever arise anew concerning the curability of amyloid liver. If we suppose that there is restoration to health of the amyloid liver, we must take it for granted that there is reabsorption of the amyloid masses and regeneration of the destroyed liver-cells. Both suppositions are in themselves admissible; for the example given by us above, of a tumor which was developed in a highly degenerated liver, and thus caused the disappearance of the amyloid matter, shows that amyloid matter can be absorbed promptly and in a considerable amount; and the regeneration of liver-cells may be seen to occur tolerably often after atrophic processes of various kinds. But now, when a liver which is too large and too firm diminishes in size under a certain course of treatment, the question is whether it is really amyloid matter that disappears. Perhaps no such matter was present, but was merely erroneously supposed to be there; perhaps it is not the amyloid matter that disappears, but the fat—or the conditions of the organ may be changed in some other way. Frerichs himself states that the diminution in the swelling of the liver does not always lead to recovery. This is readily understood after what has just been said; the liver may grow smaller, while the amyloid degeneration of the same still advances.

The *prognosis* of amyloid liver may accordingly, under all circumstances, be designated as unfavorable. If the degeneration of the liver is sufficiently well marked to be diagnosticated, death may generally be expected within the course of some months. It is, of course, an unfavorable circumstance if the causative primary affection continues to develop its influence upon the organism. How long it would take the amyloid liver of itself to bring about a fatal termination, we cannot say. If the spleen and kidneys are involved in the degeneration, the end will come so much the sooner.

Therapeutics.

General experience teaches that, when once well-marked and distinctly recognizable amyloid liver is present, there is virtually no prospect of arresting the further progress of the disease, much less of effecting recovery. Inasmuch, then, as we are helpless over against the fully developed disease, the efforts of the physician will have to be directed toward preventing the rise of amyloid liver, or postponing its development. With this view, he must strive, with all the means at his command, to combat and limit, and especially to shorten, the course of those processes of disease which notoriously bring amyloid degeneration in their train. This, it is true, can be accomplished only in certain of the diseases referred to; in others it is impossible. We shall be able, in particular, under some circumstances, to cut short, by an appropriate operation, chronic diseases of bones and joints associated with abundant suppuration; to cause the cicatrization of chronic ulcers of the skin by systematic treatment, and to combat constitutional syphilis. In all these primary affections, even if they are themselves not curable, it will be necessary, furthermore, to pay the greatest attention to the state of the general nutrition; for it is reasonable to suppose that, if nutrition is maintained at a tolerably good standard, if the cachexia is postponed, and the general anæmia and hydræmia is prevented, the chances for the occurrence of amyloid degeneration will be diminished, notwithstanding the continued losses of the juices and of albumen.

When the evidences of amyloid liver are present—that is, particularly, when a hard intumescence of the liver has been developed—we may still make the attempt to counteract the swelling by medicinal means; but even now our main duty will still consist in improving the general nutrition by dietetic measures. The diet of such persons should be nourishing and easily digestible, chiefly a meat diet. They should be warmly clothed, and kept in a pure and mild atmosphere. If circumstances admit of it, the patients may be advised to take moderate exercise in the open air. Otherwise, the treatment may be said to be essentially symptomatic. The threatening anæmia and hydræ-

mia are to be treated with preparations of iron, in addition to the dietetic care. All attention is to be given to regulating the secretions of the skin, the bowels, and the kidneys. Constipation may be combated by means of rhubarb, aloes, and similar remedies. The diarrhœa arising in the later stages of amyloid liver may be sought to be restricted by the use of astringents and small doses of opiates. Warm baths are indicated in albuminuria, and to further the secretions of the skin.

According to the experience now before us, the *indicatio morbi*, which aims at the diminution of the size of the enlarged liver, is best fulfilled by the iodine preparations, especially the iodide of potassium and the iodide of iron in the form of the syrup of that name. These remedies are especially applicable to cases of amyloid liver dependent on syphilis. Aside from these, the ammonio-chloride of iron has also been recommended. Budd saw good results from the chloride of ammonium, in doses of from five to ten grains three times a day. But, inasmuch as these salts, as well as the stronger alkaline waters of Carlsbad, Vichy, Marienbad, etc., which are so liable to be called into requisition in enlargements of the liver of every kind, may very readily cause exhausting diarrhœas, their employment should at least be carefully watched. The mild, alkaline thermal waters of Ems, as well as the sulphurous mineral waters, are less objectionable, and are therefore worthy of preference in the treatment of amyloid enlargements of the liver.

FATTY LIVER.

(Fatty Infiltration—Fatty Degeneration of the Liver—Hepar Adiposum.)

Gorup-Besanez, Lehrb. d. physiol. Chemie. 3te Aufl. Braunschweig, 1874, p. 171 (with numerous references to the literature of the physiological chemistry of the fats).—*Voit*, Ueber Fettbildung im Thierkörper, in the Zeitschr. f. Biologie, V., p. 79; furthermore, a series of other articles on the same subject by *Voit*, *Pettenkofer*, *Hofmann*, *Subbotin*, *Foerster*, and others, in the same periodical.—*Franz Hofmann*, Der Uebergang der Nahrungsfette in die Zellen des Thierkörpers. Habilitationsschrift. München, 1872.—*Radziejewsky*, Experim. Beiträge zur Fettresorption. Virchow's Arch. XLIII., p. 268, and LVI., p. 211.—*Perls*, Lehrb. d. allgem. Pathologie. Stuttg., 1877, p. 169 et seq.—*Cohnheim*, Vorlesungen über allgem. Pathologie. Berlin, 1877. I., p. 536.—*Louis*, Recherches sur la phthisie. 2. éd. Paris, 1843, p. 116.—*Lereboullet*, Mémoire sur la struct. int. du foie et sur la nature de l'altération connue sur le nom de foie gras. Paris, 1853.—*Addison*, Observations on Fatty Degeneration. Guy's Hosp. Rep. I., p. 476.—*Frerichs*, Klinik d. Leberkrankheiten. I. Braunschweig, 1858.—*Murchison*, Clinical Lectures on Diseases of the Liver. London, 1868.—*P. Mueller*, Die acute Verfettung der Neugeborenen, in Gebhardt's Handbuch der Kinderkrankheiten. Tübingen, 1877. II., p. 186.

Fatty liver depends on the accumulation of fat, in the form of larger or smaller drops, in the interior of the parenchymal cells of the liver. Such accumulations of fat are met with in the liver not only with remarkable frequency, but under the most varied external as well as internal circumstances. Fatty liver by no means only occurs under conditions which we must designate as diseased, or even under those which might fall under the suspicion of being so, but is also found in quite healthy individuals. It is just among the latter class that under certain circumstances a more or less considerable amount of fat is so uniformly to be found in the liver-cells as to justify the supposition of the liver

being one of the natural reservoirs, or normal seats of deposition, of the excess of fat present in the body, just as we find a physiological fat-depot in the subcutaneous cellular tissue and in the marrow of bones. It will only depend upon the quantity of the fat present, and probably still more on the causes and the accompanying circumstances of the accumulation of fat in the liver, whether, in any individual case, we are to regard the fatty liver as a pathological condition or otherwise.

In its chemical composition the fat accumulated in the fatty liver is not to be distinguished from the fat occurring in other portions of the body. All the fat in the human body is a mixture of the three glycerides, tripalmitine, tristearine, and triolеine. According to the preponderance of the one or the other of these three components, the fat shows a greater or lesser tendency to solidification. For the palmitine and stearine are substances that remain solid at the temperature of our bodies, but are kept fluid by the oleine. The fact that the fatty liver is sometimes peculiarly stiff, of an almost waxy quality, may depend on the preponderance of the crystallizable glycerides, especially the stearine.

So far as the origin of the fat in the liver-cells is concerned, it is either brought to the latter with the blood, or it originates in the interior of the liver-cells themselves from the albumen belonging to them. In the first instance, where to the fixed proportion of albumen in the cell a plus quantity of fat is added, we have to deal with the process which is generally designated as *fatty infiltration*. In the second instance, on the contrary, a non-nitrogenous group of atoms, viz., fat, is separated from the albumen of the liver-cells, and we are in the habit of designating the process as fatty metamorphosis, or *fatty degeneration* of the cells. But if, in the latter instance, that amount of albumen which was used up in the formation of fat is at once supplied to the cell again, the normal proportion of albumen of the cell being thus maintained and the fat lying unconsumed in the cell, then entirely the same result is accomplished as in fatty infiltration by the bringing of fat from without. It is of course a different matter if the albumen expended in the preparation of fat is not at once restored; then a condition of atrophy of the cell results,

and such a condition of fatty atrophy is generally had in view when we speak of fatty degeneration of the cells, etc.

It is at once evident that in any individual case it will be impossible to determine whether the fat which is present in the liver-cells was deposited there by the blood, or whether it originated within the cell from the albumen of the same, so long as the proportion of albumen of the cells has been restored to its original normal amount. The question may be asked whether we possess any unequivocal tests whereby we may determine that the accumulation of fat within the liver-cells possesses the significance of fatty atrophy. This question must be answered in the negative. It has hitherto generally been attempted to draw the distinction between fatty degeneration and fatty infiltration on the supposition that in the former the fat occurred in the form of very minute and numerous granules or little drops, while in the latter there was a smaller number of larger drops, and finally only one single fat-drop to be found. But it was found necessary to abandon this microscopic distinction as invalid, and particularly inapplicable to the liver. Both in fatty infiltration and in fatty degeneration, single, extremely minute fatty granules first appear in the cells, increasing in numbers while at the same time each granule increases in size. The smaller grains presently flow together into somewhat larger drops, whose number is, of course, smaller, and finally the drops unite into a single large globe, which distends the cell and gives it a roundish form. In the liver, in particular, these relations are to be observed in a very marked manner, for here, under conditions of an unquestionably degenerative nature, the cells appear filled with large drops of fat (for instance, in acute phosphorus-poisoning); while at the beginning of fatty infiltration the fat *must* be present in a state of the finest subdivision, therefore, in the form of the most minute granules, as it is a physical impossibility for fluid fat to pass directly (that is, without a special form of subdivision) and in a mass through the membranes of the vessels and cells, saturated as these membranes are with water.

Perls[1] has made the attempt to arrive at the distinction be-

[1] Lehrb. d. allg. Pathol., p. 171.

tween fatty infiltration and fatty degeneration by means of a chemical analysis, determining the amount of fat, of water, and of non-fatty solid matter in the organs in question (the liver and heart). Aside from the quantity of fat, which is much greater in fatty infiltration than in fatty degeneration, it proved that in the latter there was a diminution of the solid (non-fatty) matter, that is, therefore, of albumen, while the amount of water in the liver remains normal. In fatty infiltration, on the other hand, the fat is increased mainly at the expense of the water, the watery constituents of the liver falling from 77 to 50 per cent. or even more below the average normal standard, while the amount of non-fatty solid matter, therefore of albumen, undergoes no material change.

We have spoken of the liver as a natural fat-reservoir of our bodies. It serves as a seat for the deposit of that fat which the organism does not at once consume, and consequently lays up as reserve material for future times, in order to employ it again for its own purposes at the appropriate moment. The circumstance that the liver-cells are saturated with bile, which, according to all experience, materially facilitates the passage of fluid fat through animal membranes, makes the liver especially qualified for the reception of the fat brought to it with the blood. The rôle of a fat-depot is sustained by the liver in common with other organs, especially with the subcutaneous cellular tissue and the marrow of the bones. The organs mentioned, however, are by no means always employed to a like degree as depositories for fat. The subcutaneous cellular tissue, as a rule, is employed earlier and to a greater degree for this purpose than the liver. Where the accumulation of fat takes place as the result of over-abundant nutrition, the liver not seldom remains entirely free from fat, while a heavy layer of subcutaneous adipose tissue is developed. But under like circumstances, again, other individuals not only grow generally fat, but at the same time acquire a highly fatty liver. We are not able to render account to ourselves of the cause of this manifestation. In certain wasting diseases the layer of fat under the skin and elsewhere may even be seen to disappear, while at the same time a high degree of fatty infiltration of the liver takes place, a phenomenon the explanation of which we shall have to enter into below.

Similar conditions are to be met with in the animal kingdom. In dogs and hogs that accumulate much fat from over-feeding, this is almost exclusively deposited in the cellular tissue, while the liver goes empty. In some fishes, on the contrary, the liver is the favorite fat-reservoir, while the remainder of the body appears very poor in fat. In some hibernating animals a mass of fat accumulates in the liver during the autumn, which is gradually used up during the course of the winter.

Under normal circumstances, in man, the liver only periodically acts as a fat-reservoir; the fat accumulated therein is liable to disappear again after a longer or shorter interval. We are not quite clear as to where the fat goes or what becomes of it. Very likely a great part of it returns into the blood again, and is there further oxidized, that is, used for the production of heat. Another portion thereof passes over into the bile in the form of a solution or emulsion.[1] Perhaps fat may also be employed in the preparation of certain specific ingredients of the bile, choleic acid having been especially thought of in this connection. The latter is, however, doubted, on the ground of theoretical chemistry, because the atomic structure of the molecules in question makes the origin of that acid from fat appear improbable.

The general conditions which might lead us to expect the accumulation of fat in the liver-cells are its not immediately undergoing combustion in an amount equal to that in which it is developed, or gathered at the point named. The last cause of the imperfect combustion of fat is the insufficient supply of oxygen. In this respect the liver appears as a place quite peculiarly fitted for the storage of fat. For the liver, even under normal circumstances, receives a comparatively very small amount of oxygen with its blood, the blood of the portal vein, which is the chief

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[1] According to the observations of *Frerichs*, *J. Ranke*, and *Jacobsen*, the quantity of fat excreted with the bile is liable to great variations. About one-fifth or one-sixth of the solid constituents of the bile consists of fat and cholesterine. If, according to *J. Ranke*, an average of 15.32 c. ctm. of bile, with 0.44 grm. of solid constituents, is secreted in the course of twenty-four hours for every kilogram of a man's weight, then a man weighing 130 pounds would daily furnish 28.C0 grm. of solid bile, 5 to 6 grm. of which would be fat and cholesterine. (Compare *Gorup-Besanez*, Lehrb. d. phys. Chemie, 3te Aufl., 1874, p. 534.)

element in the case, being pre-eminently poor in oxygen. Under pathological conditions the quantity of oxygen may be still further reduced: for instance, when there is a lack of red blood-corpuscles, of oxygen carriers, and therewith the chances for the consumption of fat in general, and consequently also of liver-fat, are still more diminished. But a circumstance which might have even more weight than this, so far as liver-fat is concerned, is the activity of the production of bile. If the secretion of the liver is abundant, a sufficient method of escape is thereby opened to the fat accumulated in the liver-cells; if, on the contrary, it is habitually diminished, as is the case where there is a well-marked tendency to corpulence, or becomes so by reason of disturbances of digestion, then the prospects for the consumption of the fat are but slight.

It will make itself apparent that in the production of fatty liver all the conditions here referred to come into operation, both those which relate to the bringing and the development of fat and those which relate to the consumption of the same, especially to fat-combustion, but that they do not in all cases work together in the same way, inasmuch as, in any individual case, sometimes the one and sometimes the other factor is of preponderating significance.

Etiology.

1. The development of fatty liver is very greatly influenced by the method of nourishment—the diet—of the individual. Among the various factors that come into play in this connection, one of the first to be considered is *the amount of fat in the ingesta.* The idea very naturally suggests itself that if the food be very rich in fats, a part of the latter might pass over without any change into the natural fat depots, therefore also into the liver. Numerous phenomena in the domain of the physiology of nutrition seem to find their simplest and least forced explanation on this hypothesis. Magendie already discovered that dogs who are fed exclusively on butter acquire a very fatty liver, while at the same time large quantities of fat are expelled through the sebaceous glands of the skin. More recently other

observers have repeated this experiment with manifold variations, always arriving at the same result. Frerichs, in particular, while feeding dogs with fat, has made the changes going on in the liver-cells the subject of direct microscopic observation, cutting out minute portions of the livers of such animals, both before the experiment and during the progress of the same, and testing the liver-cells as to the amount of their fatty contents. The circumstance that a fatty liver, which afterward disappears again, is quite commonly developed in children during the period of suckling, that is, when on an exclusively milk diet, corresponds with these experiments on animals; as does the fact that a similar condition is developed under the use of large doses of cod-liver oil. But on looking at the matter more closely, it does not seem justifiable to conclude that because much fat is introduced with the food, and a fatty liver is developed at the same time, therefore the fat appearing in the liver is to a certain or to a great extent to be regarded as the direct fat of the food. For it might be possible that all the fat appearing in the liver originated from the albumen, and that all the fat of the food, after having been oxidized, might have entirely disappeared from the juices of the body. This suspicion, justifiable in itself, has, however, been set aside by the investigations of Fr. Hoffmann[1] and Radziejewsky.[2] They have demonstrated with perfect clearness that a part of the fat introduced with the food is certainly deposited unchanged in the natural fat-depositories, and, among others, in the liver.

But our organism is capable of accumulating fat when none is brought to it in the food; it is able, therefore, to form fat of itself, and, according to all appearances, the quantity of fat thus produced is much more considerable than that which is directly introduced with the food. Until within a few years it was regarded as an established fact that the formation of fat took place principally at the expense of the carbo-hydrates introduced with the food. But more recent investigations in the domain of the nutritive process, and especially the labors of the physiologists

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[1] Der Uebergang der Nahrungsfette in die Zellen des Thierkörpers. München, 1872.

[2] Virchow's Archiv, XLIII., p. 268; and LVI., p. 211.

of Munich, have effected a radical change in the views on this subject. Chemists now consider it as highly improbable that fat is ever produced from the carbo-hydrates, while it is regarded as almost certain that all fat developed during a non-fatty diet is produced from the albumen of the latter. During the breaking up of a nitrogenous compound, which eventually, after all sorts of changes, leaves the body with the urine (as urea and the like), fat is formed from the albumen, the fat being destined for combustion, and, having gone through various intermediate steps, being finally oxidized into carbonic acid and water. We cannot definitely state in what organs and tissues this breaking up of albumen and formation of fat take place; probably, however, these processes take place everywhere in the body, in all organs and tissues. But if the carbo-hydrates do not directly participate in the formation of fat, there is no doubt whatever that the accumulation of fat by the organism is favored by a diet rich in carbo-hydrates. The part they take seems to consist in their drawing the available oxygen in the body to themselves, with a certain predilection therefor, so that no oxygen is left over for the combustion of the fat produced from the albumen, and this fat must therefore be conveyed uncombusted to its places of deposit.

We thus see the body accumulate fat under a good and abundant supply of nourishment, but, of course, only on the supposition that the fat which has resulted from the breaking up of the albumen, or that introduced with the food as such, is not at once burned again. There must be a disproportion between the development of fat and the combustion of fat; the latter must fall behind the former. In fact, it is not necessary that there should be any downright excess in the amount of nourishment introduced, the rule being, rather, that if any one eats more albumen and fat than is requisite for the maintenance of his standard in these things, the surplus will be accumulated as fat whenever the supply of oxygen is not increased to a corresponding degree.

But this very matter of the consumption of oxygen is one in which the greatest differences exist in different individuals even within the limits of health. In the man who devotes himself to a quiet and easy life, avoiding bodily as well as mental exertion,

the entire amount of tissue-metamorphosis, and consequently the supply of oxygen, will be diminished, and the chances for the accumulation of fat increased. If at the same time a largely increased supply of nutritive material takes place, then the accumulation of fat must be excessive, while, with an active life and sufficient bodily exertion, the supply of oxygen is sufficient to burn entirely all the fat originating from the food, directly or indirectly. A man who takes but little exercise while consuming abundant nourishment, is under conditions similar to those in which we place an animal which we intend to butcher. Such animals are not only abundantly fed, especially with carbohydrates, but their movements are also limited—they being kept in their stalls—and the endeavor is also made to keep the stables as warm as practicable; warmth, for evident reasons, diminishing the amount of oxygen consumed by the animal.

But it is an old piece of experience that all persons do not behave in the same manner when subjected to the influences under consideration. Under the same circumstances, with the same diet and the same amount of bodily exertion, some persons grow fat, and, in particular, develop a large, fatty liver, while others remain lean, and their liver appears almost free from fat. We therefore attribute to the first a tendency, a predisposition, to corpulence and to fatty liver. In some families we see this tendency to corpulence handed down from one generation to another. It is hard to say wherein the greater tendency of certain individuals to corpulence consists; still, we suppose that it is not so much in a difference as to the amount of nourishment consumed and absorbed as it is in an abnormally slight combustion of the fat on hand. This might be owing to the fact that, in such persons, all processes of oxidation in the body are carried on with an abnormally small degree of energy. The fault would therefore lie in the tissues, and consists in the fact that these offer abnormally great resistance to the assaults of oxygen. At the same time, in the matter of corpulence it is not merely a question of individual predisposition, for general influences also make themselves felt, the *modus operandi* of which is anything but understood. Under this head we may mention sex, women being decidedly more disposed to corpulence than men; also age, the

tendency to grow fat being most pronounced during middle age. Even climate is said to exert some influence, a temperate, moist climate being favorable to fatness.

In most cases in which fatty liver is to be principally attributed to the diet, some other additional causes can also be designated which operate favorably to the production of fatty liver, generally by limiting the destruction of fat. Among such favoring circumstances we may mention the lack of bodily exercise and the abundant introduction of carbo-hydrates (sugar) in nurslings, who owe their fatty liver to an exclusively milk diet. In slothful persons, especially in women who are inclined to be stout, the indisposition to exercise comes very decidedly into play. Women who are inclined to be corpulent are very often anæmic at the same time, and the consequent diminution in the interchange of gases in the body interferes with the combustion of fat. Finally, experience shows that in fat persons the secretion of bile is too small, consequently in this way also too little fat is carried off, and the accumulation of fat in the liver is favored.

2. Fatty liver, furthermore, very often arises in connection with certain pathological processes which, without having anything to do directly with the liver, cause a profound disturbance of the entire organism. The extremely frequent coincidence of fatty liver with pulmonary consumption is universally known, but no better known than the fact that fatty liver may just as well be associated with other wasting diseases, as, for instance, with the cancerous cachexia, with chronic ulceration of bones and joints, with chronic dysentery, etc. The connection here referred to is expressed in the term "cachectic fatty liver." At the first glance there is undeniably something surprising and apparently paradoxical in the fact that a condition which is known as the usual result of an unduly abundant supply of nourishment, and therein finds its natural explanation, should likewise arise in just the same form under apparently opposite conditions—that is, with lowered nourishment, general emaciation, and cachexia. Various attempts have been made to explain this striking phenomenon. In so doing most writers have gone on the supposition that the immediate ground of an accu-

mulation of fat in the liver could only lie in the insufficient combustion of fat, as there could be no thought of increased *fat development* in the organism in a patient suffering from progressive emaciation. But the cause of the incomplete combustion of fat was thought to be due to the lack of oxygen, which in consumptives seems to be most easily explained by the lowering of the respiratory process caused by ulcerative destruction of the lungs. An objection urged against this view is to the effect that the fatty liver is not only met with in phthisical persons—that is, in those whose lungs are destroyed—but that other wasting diseases, in which the lungs remain intact, likewise give occasion to the rise of fatty liver. If, therefore, the lack of oxygen were the cause of cachectic fatty liver, this lack of oxygen would have to be based on conditions other than the anatomical lesions of the respiratory apparatus. Another objection to the method of explanation attempted above consists in the fact that in various diseased conditions in which the interchange of gases is decidedly disturbed, and the taking up of oxygen is diminished—as, for instance, in emphysema of the lungs, in stenosis of the larger air-passages, in curvature of the spine, etc.—no fatty liver is developed. This objection, however, appears to have but little weight, for we must remember that our organism presides over various compensatory arrangements by means of which the requisite amount of oxygen is pretty sure to be introduced into the body, in spite of the mechanical hindrances to respiration that may be present. In such cases the supply of oxygen to the tissues cannot readily be lowered below the amount required, as long as the general strength of the patient is well preserved. At all events, we may declare without hesitation that the fatty liver of consumptives cannot depend only on the destruction within the lungs.

Others, again, consider that, in the explanation of cachectic fatty liver, special regard is to be paid to the composition of the blood. The blood in consumptives (as well as in inebriates) very often shows a milky, turbid quality, which depends on an abundant admixture of finely subdivided fat with the blood-plasma, and which is generally designated as lipæmia or galactæmia. The great wealth of fat in the blood of phthisical patients de-

pends on the fact that in the progressive emaciation of such persons the fat previously stored in the subcutaneous cellular tissue is taken up into the blood to be further expended, according to the necessities of tissue metamorphosis. But, as the combustion of the fat contained in the blood cannot be completed on account of disturbance of the respiratory apparatus, or for other reasons, the uncombusted surplus of fat is temporarily deposited in the liver. The entire process is thus represented as being a sort of physiological fat-metastasis. The view here set forth of the origin of fatty liver in pulmonary consumption is said to have been first announced by Larrey. It found influential supporters in Budd and Frerichs ; but certain objections can also be urged against it, and, in fact, it seems very questionable whether this theory exhaustively explains the whole process. It cannot be accurately demonstrated that the fat mingled with the blood of consumptives is derived from the subcutaneous cellular tissue. It is hard to understand why the emaciation—consequently the disappearance of fatty tissue—progresses when there is no need of fat for tissue-metamorphosis, but even a surplus of the same on hand, which the blood has to be freed from through the intervention of the liver. In the lipæmia of consumptives, according to the theory given above, there would be a mere change of place of the fat, for which we can see no necessity. Another possibility is therefore worthy of being put to the test, viz., whether in the fatty liver of cachectic persons, in addition to the factor of incomplete combustion of fat, which undoubtedly exists, another cause may not also be included, viz., the too abundant production of fat in the organism.

That the consumptive suffers great losses of tissue is a fact as unquestionable as that he is unable to overcome these losses by the nourishment introduced. The fact of the emaciation, of the loss in weight, is the unequivocal evidence hereof. But if the introduction of nourishment is not enough to meet the requirements, the organism must seize upon its own components of albumen, fat, etc.; the current expenditures are, to a certain degree, met at the cost of the substance of the body, of the tissues, and it appears as if all the tissues were thus involved, although to very different degrees. Now just as a well man, on a rich and

abundant diet, forms fat from the albumen of his food, so the patient who is emaciating forms the same from the albumen of his body; he produces fat while he sacrifices albumen. The simultaneous disappearance of the fat from the cellular tissue is only in apparent conflict with the theory of increased fat-production from the body-albumen which falls a victim to consumption. Both processes take place independently of each other. The disappearance of adipose tissue is the expression of the general consumption; there is no intimate connection whatever between this manifestation and the somewhat accidental fact that fat is formed from the breaking up of albumen.

The fat present in the blood of consumptives, which we take it for granted is deposited in the liver, might, therefore, well originate from various sources. It may come in part, directly or indirectly, from the food; it is also, in part, the fat formed from the breaking up of the albumen of the organism; while, finally, it is in part taken up from the disappearing adipose tissue. If we are, therefore, unable to see plainly how much is to be attributed to one or another source of fat, this much, at least, is all the more settled, that in pulmonary consumption the combustion of fat is incomplete. The immediate reason for this is, of course, the deficiency in oxygen; but, as already indicated, the explanation of the latter lies less in the anatomical lesions of the lungs than in the fact that, corresponding to the degree of the consumption, the functional capacity of the tissues and organs has materially suffered. The result thereof is diminished tissue-metamorphosis and a weakened interchange of gases in the tissues, all of which furnishes the conditions for the diminished introduction of oxygen. But the consumption also affects the formed constituents of the blood, and the destruction of numerous red blood-corpuscles, which serve as oxygen carriers, must be taken into consideration as a further cause for the limited combustion of fat.

The uncombusted fat is, therefore, met with again in the fatty livers of consumptives. The development of the same is influenced by the state of the digestion. The more favorably digestion progresses the more abundant is the formation of bile, and therewith the consumption of fat within the liver. If, on the

contrary, digestion is disturbed, the secretion of bile is lessened and the accumulation of fat within the liver becomes quite excessive. Nor is it a matter of indifference, so far as the degree of fatty liver to be developed is concerned, how large an amount of subcutaneous adipose tissue existed before the occurrence of emaciation. The greater the amount of fat that has been absorbed from the cellular tissue during the progress of the consumption, the more of it shall we meet with in the liver. In phthisical women, therefore, in whom the adipose layer is more largely developed than in men, the fatty liver attains a particularly high grade of development.

The fatty liver which is developed in other wasting diseases is to be explained in the same way as in pulmonary consumption; but it is to be remarked that it does not occur as constantly, nor, on an average, attain as high a grade in other wasting diseases as in phthisis, which may be partly explained by the condition of the respiratory organs, and partly by the degree of the cachexia. Fatty liver is observed in the consumption following cheesy inflammation and ulceration of the bones and the lymphatic glands, following intestinal phthisis, or exhausting, tedious suppurations of the bones and joints, or chronic dysentery, or in the cancerous cachexia, and in the extensive bed-sores following myelitis and similar disturbances. The cachectic fatty liver is very liable to occur in those changes of the blood which cause a material diminution in the amount of hæmoglobin it contains; therefore in the various forms of anæmia—both that which arises from a single severe hemorrhage or oft-repeated losses of blood, and the progressive pernicious anæmia developed idiopathically; likewise, although in a less degree, in chlorosis and leucæmia. Under these circumstances the fatty liver is manifestly the expression of defective combustion of fat, which itself, again, depends upon a deficient supply of oxygen. It is not to be assumed, in such cases, that the lowering of the supply of oxygen necessarily runs parallel with the diminution in the number of red blood-corpuscles, because it has been demonstrated that even where there is a diminished number of red blood-corpuscles the interchange of gases may take place to the extent of the original normal limits, the blood-corpuscles that

are present, so to speak, assuming the labor of those that are wanting. This is the case in chlorosis and leucæmia; and hence, in these conditions, the combustion of fat is generally not noticeably altered; fatty liver is more rarely developed, and then only a low grade of the same. But in course of time, under the conditions of anæmia as the result of faulty nutrition, the functional capacity of the organs is also lowered, their consumption of oxygen is limited, and, corresponding to this, the supply of oxygen to the blood and the tissues remains within abnormally low limits. Then, for the first time, we have the conditions implying defective combustion of fat, and, after a while, fatty liver.

3. Fatty liver is of frequent though not constant occurrence among *habitual drinkers*, especially where the actual *dyscrasia of inebriety* exists. Here the fatty liver attains a very high grade, is occasionally also associated with proliferation of the interstitial connective tissue, so that the liver appears harder or even presents the characteristic qualities of actual cirrhosis (cirrhotic fatty liver). In view of the lipæmia which is present at the same time, the fatty liver of hard drinkers may certainly be regarded as fatty infiltration; and when we take into account the method of life of habitual drinkers, who generally take but very little solid nourishment, we shall have to consider the wealth of fat in the blood, not so much as being the expression of increased fat production as it is of incomplete fat combustion. The cause of the latter is the excessive indulgence in alcohol. It is demonstrated that alcohol lowers the processes of oxidation in the organism, that it diminishes the excretion of carbonic acid and the introduction of oxygen. If we imagine that alcohol renders the tissues more capable of resisting the aggressive influence of oxygen, then, as Cohnheim (loc. cit., p. 554) has indicated, the growing fat of habitual drinkers might be regarded as parallel with obesity on constitutional grounds, where we may take for granted a similar relation of the tissues to oxygen. The arrest of the fat in the liver is favored, in topers, by the diminished energy of the digestive processes. In such persons, digestion and the preparation of bile are greatly disturbed; the avenues of escape for the liver-fat are therefore in part destroyed.

4. Fatty liver is one of the most prominent manifestations of *acute phosphorus-poisoning.* There has been much debate as to whether the liver of phosphorus-poisoning is the seat of fatty degeneration or fatty infiltration of the liver-cells. The fact that the fat in the liver-cells is in the form of large drops, as well as the entire appearance and other physical conditions of the fatty liver of phosphorus-poisoning, has been looked upon as evidence of the identity of the same with the ordinary infiltrated fatty liver of gluttons and drunkards. But the anatomical condition of the other organs—the thick dissemination of *finely* granular fat throughout the muscular fibres of the heart, the gastric gland-cells, and the renal epithelium—as well as the external circumstances to which the fatty liver of phosphorus-poisoning owes its origin, indicates with great certainty that the origin of the fat within the liver-cells depends on a degenerative process. Perhaps the saturation of the liver-cells with bile is the reason why the fat in the interior of the same is not found in a state of finely granular subdivision, but immediately runs together in larger drops. When incorporated with the juices of the body in sufficient quantity, phosphorus causes the gravest changes in the general metamorphosis of tissues; the consumption of oxygen and the excretion of carbonic acid are materially diminished, as has been proved by Bauer;[1] indeed, they may sink to half of their normal standard. At the same time, an increase in the decomposition of albumen takes place, and we see the excretion of urea rise. The fat resulting from the acute decomposition of albumen in the tissues is left lying there uncombusted, inasmuch as the oxygen required for this purpose is not forthcoming; we therefore find the liver-cells, the muscular fibres of the heart, and other parenchymas in a state of fatty degeneration. The fact that in these cases fatty infiltration of the liver is out of the question is proved by the experiment of Bauer (loc. cit.), who saw the most well-marked fatty liver, as well as fatty degeneration of other parenchymas, developed in a dog poisoned with phosphorus, although he was absolutely starved after the poisoning and had previously, as far as possible, been robbed of any

[1] Zeitschrift f. Biologie. VII., p. 53.

reserve supply of fat by prolonged fasting. The fat in the liver must therefore have originated from the albumen of its cells.

5. Fatty liver is one of the manifestations of the so-called *acute fatty degeneration of the new-born.*[1] This disease has hitherto but rarely been observed in man, but it is quite frequent among our domestic animals, especially among young pigs, lambs, and colts (the so-called foot-halt), among whom it causes great devastation. The disease is anatomically characterized by fatty degeneration of the heart, of the muscles of the body, of the liver, and the kidneys; the causes thereof are, however, for the present shrouded in the profoundest obscurity. Here too, as in phosphorus-poisoning, there seems to be increased decomposition of the albumen of the tissues, with a simultaneous defective supply of oxygen. The disease has also been observed in puerperal women in a manner quite similar to that in which it occurs in the newly-born.[2]

In all the cases which have thus far been alluded to, we have been able to show the dependence of the fatty liver on etiological conditions which affect the entire organism, on abnormal conditions of the general tissue-changes of the body. The fatty liver has therefore thus far always shown itself as the expression of a general constitutional malady. But there are also

6. Cases where the accumulation of fat in the liver-cells has the significance of a purely local process, viz., that of fatty atrophy (fatty degeneration). This is especially true of the *fatty nutmeg-liver* of patients with heart disease. This is to be explained on the ground that the long-continued venous congestion causes a diminution of the arterial influx, as well as of the current of juices passing through the tissues. The fat which is produced within the liver-cells by the breaking up of albumen does not undergo combustion, by reason of the lack of oxygen; it is likewise not carried away, on account of the weakened current

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[1] *P. Mueller*, Die acute Fettentartung der Neugeborenen (in Gebhardt's Handbuch der Kinderkrankh. Tübingen, 1877. II., p. 186). *Hecker* und *Buehl*, Klinik der Geburtskunde. I. 1861, p. 296.

[2] *Hecker*, Beiträge zur Lehre von der acuten Fettdegeneration der Wöchnerinnen und Neugeborenen (in the Monatsschrift f. Geburtskunde, XXIX., p. 321). The same, Arch. f. Gynäkol., X., p. 537.

of juices, but accumulates in the interior of the cells. But, for the same reason, the disintegrated albumen of the cells is not replaced to a sufficient extent; the cells are therefore left in a state of fatty atrophy. The same process may be observed, to a more limited extent, in the neighborhood of tumors—for instance, of cancerous nodules—within the liver. Such tumors sometimes appear enclosed in a narrow zone of pale liver-tissue very rich in fat, while the remainder of the liver-substance may be quite free from fat. Here it is the pressure of the tumor on the blood-vessels which disturbs the current of fluids, causing a local lack of oxygen, and therewith fatty degeneration.

Frequency of Fatty Liver.—After all that has been said of the causes that may lead to fatty liver, we shall not be at all surprised to learn that higher as well as lower grades of fatty liver are extremely common. At the post-mortem table, in particular, we shall meet with fatty liver much more frequently than clinical observation alone would have led us to expect. The attempt has been made at various times to determine, in numbers, the frequency of fatty liver. We shall not be surprised that very varied results have been arrived at, if we remember that the lower grades of fatty accumulation can only be recognized by the microscope, and are therefore often entirely overlooked; that, furthermore, differences exist in different regions of country, on account of dissimilarity in the methods of life; and, finally, that the populations of different hospitals are very variously constituted. The figures given are therefore entitled to no other value excepting as they give us, in a very general way and in rough outlines, an idea of the enormous frequency of fatty liver. Frerichs examined 466 bodies with reference to this point. Among these he found 28 cases of fatty liver of the highest grade, and 164 other bodies (therefore nearly one-third of the entire number) with livers generally rich in fat. That there should be such a large number of cases of this latter class is owing to the large number of consumptives which happened to be comprised in the 466 cases. Fatty liver was found more frequently in the female sex than in the male: the proportion in the former was $1 : 2\frac{2}{10}$; in the latter $1 : 3\frac{5}{10}$. Fatty liver was found quite often in persons who were the victims of some sudden acci-

dent, and otherwise quite well ; in children at the breast, or who were otherwise kept on an exclusively milk diet ; in pregnant and puerperal women. It was, furthermore, observed in connection with the most varied conditions of disease, but in no disease more frequently than in pulmonary phthisis. Of 117 tuberculous patients, 17 had fatty liver of the highest grades ; in 62 other bodies of this category there was a liver rich in fat ; and here, too, the female sex was in the predominance. The same condition of things exists in the alcoholic dyscrasia ; of 13 persons who died in the accidents of delirium tremens, 6 had a liver very rich in fat, in 3 there was a little fat, in 2 none at all ; 2 others had cirrhosis of the liver. The statistics given by Louis[1] are very different from the above. Among 230 individuals who had died of various acute diseases (to the exclusion, however, of phthisis), he claims to have seen but 9 cases of fatty liver (in 7 of which there was at the same time tubercle), while among 120 phthisical patients fatty liver occurred 40 times.

Pathological Anatomy.

Fatty infiltration effects an increase in the size of the liver, which in very well-marked cases may attain double its normal dimensions. Herewith is associated a corresponding increase in the absolute weight of the organ, while the specific gravity of the fatty liver is less than that of the healthy liver ; indeed, in the worst cases it is lowered almost to that of water. As the deposit of fat takes place uniformly throughout the entire organ, it is generally not associated with any noticeable alteration in the external form of the liver. It is, indeed, stated that the fatty liver grows less in thickness than in its flat diameter, and that the right lobe therefore appears strikingly long, and reaches far downward. At the same time this is by no means uniformly the case ; sometimes the liver is found enlarged principally in its thickness. In fatty livers of a high grade, it is to be noticed that the anterior, otherwise sharp border appears rounded off and thickened. The serous covering undergoes no change in

[1] Recherches sur la phthisie, p. 116.

fatty liver; it is tense, smooth, and lustrous, and allows the parenchyma to gleam through with a pale color. Sometimes, when the circulation of blood in the liver is disturbed, one sees little, strongly injected, venous points appear under the serous capsule. The consistency of the fatty liver can only be properly estimated when the liver — that is, the whole body — is still warm, for in the cold the fat deposited in the parenchyma hardens, and the otherwise soft, fatty liver is transformed into a stark mass, offering great resistance to the knife. The fatty liver, on the contrary, while still warm, feels soft; it has a peculiar doughy consistency, and pits permanently on pressure. The fatty liver can be cut without difficulty, just like a normal liver; but a thick layer of whitish gray tallow remains clinging to the knife, and a similar tallow can be pressed out in abundant quantity by stroking the cut surface with a knife. The cut surface shows a variable appearance in different grades of fatty infiltration. In the highest grades it is, like the outer surface, of a more uniform appearance; the lobular structure of the parenchyma is obliterated; the color pale yellow to grayish white; the cut surface of a shining, fatty appearance. In less high grades the lobular structure of the liver generally appears quite plainly, inasmuch as the centre of the lobule, where the parenchyma has remained free from fat, shows a liver-brown or blood-red color, while the marginal portion of the lobule alone presents, in a more or less wide zone, the pale-yellow or whitish gray color of fatty infiltration. This is the delineation of the so-called nutmeg liver.

The amount of blood in the fatty liver appears, in general, to be very slight, at least in the dead body; it diminishes with the increase of the amount of fat. Hence, the parenchyma of the liver appears extraordinarily dry, and only the coarser vessels are seen filled with blood. In otherwise healthy individuals, however, this extreme poverty of blood appearing in the fatty liver might, to a good degree, have the significance merely of a post-mortem appearance. During life the amount of blood, under such circumstances, must certainly be greater, perhaps quite normal; for at this time the pressure exercised upon the blood-vessels by the cells filled with fat is, to a certain degree,

overcome by the counter-pressure of the blood. It is not until this counter-pressure of the blood has ceased, after death, that the compression of the capillaries by the distended parenchymal cells fully asserts itself; the blood is pressed out of the capillaries and back into the larger vessels. That the relations of the circulation in the fatty liver are during life actually as above indicated may be concluded from the fact that no greater force is required for the artificial injection of the fatty liver through the portal vein, than that which is found requisite for the successful injection of a healthy liver.

There are certainly also circumstances in which, in addition to fatty infiltration of the liver-cells, the amount of blood contained in the organ is increased; for instance, in the engorged liver of persons suffering with heart disease, etc. But even here we have fundamentally the same relations as in pure fatty liver. For in each lobule there is poverty of blood just so far as the fatty infiltration of the parenchyma extends (at the margin of the lobule); and wherever (in the centre) the engorgement with blood shows itself the fatty deposit in the cells is wanting. Thus, even in the engorged liver, anæmia goes hand in hand with fatty infiltration.

Rokitansky describes a modification of ordinary fatty liver under the designation of *wax-like* liver (wächserne Leber), by which term, however, we are not to understand the waxy or amyloid liver. This wax-like form is said to differ from the ordinary fatty liver by a deeper color, similar to that of yellow wax, by greater consistency, and the dry, friable quality of the tissue. In spite of the large amount of fat present, but little remains clinging to the knife-blade. Rokitansky explains this condition on the supposition that there is a peculiar composition of the fat. This might most readily be supposed to consist in a preponderance of the more solid fats, palmitine and stearine, over the fluid oleine.

The description of fatty liver given above is only applicable to typical cases of this condition. At the same time numerous deviations from the typical standard occur. All fatty livers are not correspondingly enlarged; they may be normal or even diminished in size. The latter is especially true of those cases of

fatty liver which are complicated with cirrhosis. Nor can a correct judgment always be formed, with regard to the fatty contents of a liver, from the color, consistency, and other physical conditions of the same. It is particularly easy to mistake a simple anæmic liver, judging by its mere looks, for a fatty liver, which it greatly resembles by its paleness and softness. On the other hand, a tolerably high grade of fatty liver may exist without betraying itself by any characteristic appearances. Full assurance of the existence of, as well as approximately of the amount, of fat, can, therefore, only be given by a microscopic examination.

Sometimes the fat is not uniformly distributed throughout the entire liver, but only deposited in isolated masses and areas. But then purely local causes lie at the foundation of the accumulation of fat, and the entire condition has more the significance of fatty degeneration than of actual infiltration. Thus we see a narrow ring of fatty degenerated liver tissue arise in the neighborhood of cancer nodules, of conglomerations of tubercles, of cicatrices, etc. Here the pressure of the neoplasm and the consequent disturbances of circulation might be the cause of the disturbed nutrition of the liver-cells and their fatty degeneration. In the combination of fatty infiltration with amyloid degeneration, which occurs so often (lardaceous fatty liver), similar local influences might co-operate in causing the deposit of fat, although in this condition there is no lack of general causes for fatty infiltration.

Disturbances of the biliary apparatus are not necessarily associated with fatty liver.

The amount of fat deposited in the tissues may assume enormous proportions. According to the table of Perls (loc. cit., p. 172), the normal proportion of fat in the liver may be estimated at about three per cent. of the weight of the organ. In drunkards and fat people the proportion of fat may be seen to rise to forty per cent., and even higher. Vauquelin determined the amount of fat in a fatty liver of the highest grade to be forty-five per cent.; in one case of Perls' it amounted almost to forty per cent. Frerichs found almost forty-four per cent. of fat in a fresh fatty liver, while in the same case the liver substance, freed from

water, consisted in seventy-eight per cent. of fat. The fact that an increase in the fatty contents runs parallel with a diminution in the watery constituents of the liver was first observed by Frerichs, and has recently been confirmed by Perls.

Microscopic examination shows at the first glance that the fat is contained in the interior of the liver-cells. The changes which the latter undergo in this process begin with the appearance of the very finest dark granules in the protoplasm of the same. These granules gradually increase in size, and soon appear as very small globules of fat, which are to be recognized by their strong refraction of light, their sharply defined dark margin, and bright, shining centre. The small fat-globules afterward flow together into a few larger drops, and, finally, all the fat in the cell is united in one large globe of fat, which distends the cell, lends it its globular form, and crowds aside the protoplasm, as well as the nucleus of the cell. In the very highest grades the liver-cell thus altered has entirely the appearance of a common fat-cell; but the nucleus of the liver-cell never entirely disappears, although it is hard to find. The quantity of the protoplasm in such liver-cells transformed into fat-bladders, as far as we are able to judge of it by microscopic examination, seems to undergo a considerable diminution. The protoplasm either surrounds the fatty ball as a narrow margin, or it appears, together with the cell-nucleus, in the form of a crescentic strip pressed close to the cell-membrane. The liver-cell, as such, is therefore not destroyed by taking up even the largest amounts of fat. It is to be presumed that it may return to its original condition after having reached any stage of infiltration. During the disappearance of the fat from the liver-cells we see the same microscopic images produced as during the rise of the infiltration, only in the inverse order.

The course of the deposit of fat proceeds quite regularly, in such manner that the cells lying at the outer border of each lobule are infiltrated first. The change advances in a radiate manner, from the periphery toward the central vein. When the deposit of fat is confined to a more or less wide peripheral zone, we see it attaining its higher grades within the latter, while the cells lying further toward the centre are likely to be quite free

from fat. Accordingly, those liver-cells which are first involved in fatty infiltration are always the first to be quite filled with fat, before other liver-cells are included in the process.

In opposition to the prevailing opinion, Perls[1] believes that the fat is not deposited exclusively in the parenchymal cells, but also outside of the same, probably in the intercellular biliary passages. He is led to this conclusion by the peculiar forms in which the fat appears when thin sections of the fresh liver are hardened in a solution of osmic acid, and the tissue is afterward dissolved out by the addition of Javelli's lye (subchloride of potassium). The rigid masses of osmium fat, which at first remain unaltered by the lye, do not appear altogether in the form of single balls, as would be the case if the fat merely lay within the cells, but also appear as rows of balls and as peculiar arborescent structures, which in some places look like the casts of fine passage-ways, the globular masses of fat being ranged along them. If fine sections of the fatty liver treated with osmic acid are examined before corrosion with Javelli's lye, similar images are obtained, but one sees the liver-cells surrounding the peculiar fatty structures. This matter certainly calls for more thorough investigation before the conditions supposed to exist can be regarded as firmly established.

Pathology.

The pathological significance of fatty liver can only be arrived at on the basis of a clear insight into the method of origin of the same, for it is only in this way that we can attain a correct view of the essential nature of the condition in question. As long as every accumulation of fat in the liver was regarded as the product of a disturbance of nutrition of the liver-cells, as the expression of fatty degeneration—a view held, among others, by Andral, Cruveilhier, Barlow, and Henoch,—it necessarily followed that the fatty liver had to be regarded in every case as a diseased manifestation. We are now agreed that this significance is to

[1] Loc. cit., p. 177. Even *Vogel* and *Wedl* asserted that the fat also occurred in the interstices of the liver-tissue.

be attached to fatty liver only in the minority of cases—for instance, in phosphorus-poisoning and the fatty nutmeg liver of cardiac disease; that, on the contrary, the most well-marked and most frequent cases—the fatty livers of gluttons, drunkards, and cachectic individuals—are those in which the liver serves as a reservoir for the excess of fat present in the body, where we, therefore, chiefly have to deal with a fatty infiltration. At the same time we have declared plainly enough, when speaking of the etiology of this affection, that the two conditions cannot be as sharply separated, even with regard to their pathogenetic bearings, as is commonly supposed. Where the liver occupies the position of a fat-reservoir, fatty liver cannot, without further ceremony, be designated as a disease, for the liver here fulfils at first only its physiological destiny, and no one thinks of seeing any indication of disease in the circumstance that the organism sometimes accumulates a supply of material which, under other circumstances, it may usefully employ for its own purposes elsewhere. A certain amount of fatty contents within the liver, which may even attain a considerable degree, is therefore quite consistent with the idea of health. On the other hand, it is evident that a fatty accumulation within the liver, when it passes beyond a certain limit, attains the significance of a disease; but it is quite impossible to designate a definite boundary line, passing beyond which the fatty liver is to be designated as decidedly diseased. This certainly does not depend only upon the amount of fat accumulated. Fatty liver may be regarded as a phenomenon consistent with health when the occasion for its development does not consist in pathological conditions of the organism; when, furthermore, it is a transitory condition, and the liver remains capable of working up the fat produced therein in the normal course of its processes, and, in fact, freeing itself of the same; when, finally, the accumulation of fat does not reach so high a grade as to react in a disturbing manner upon the functions of the liver and the organism generally, as well as upon the well-being of the individual. On the other hand, fatty liver becomes a disease not only by virtue of the great mass of the fat accumulated, and the consequent disturbance in the functions of the liver and burdening of the patient, but also, when there is

only a small amount of fat, by virtue of the fact that it owes its origin to pathological processes, and especially that it represents a condition of a permanent and even a progressive character, from which a return to the normal condition, if it is not impossible, is at least highly improbable.

So far as the effects of an accumulation of fat in the liver on the functions of the same, and indirectly on the whole organism, are concerned, daily experience teaches that the deposit of a moderate amount of fat is associated with no sort of disturbance of the liver-cells. An excessive accumulation of fat, on the contrary, such as is met with in gluttons, drunkards, and consumptives, not only interferes with the functions of the liver, but also reacts in a disturbing manner upon the entire organism, the more so because, as a rule, this condition is lasting. We are in the habit of supposing that the excessive amount of fat in the liver-cells effects a mechanical disturbance of the flow of blood in the capillary system of the portal vein, and that it renders the flow of bile from the hepatic lobules more difficult. For, inasmuch as the liver-cells are distended into great globular structures by the fat they have taken up, they press from all sides against the blood-carrying capillaries, and this pressure is the more effective as the counter-pressure on the part of the blood in the branches of the portal vein is of itself very low. Hence the simple, uncomplicated, fatty liver is always anæmic, while the trunk of the portal vein and its roots appear quite full. But the obstruction of circulation in the portal vein certainly never reaches any very high grade; fatty liver never results in ascites, nor in swelling of the spleen; at the most, the obstruction to the escape of venous blood from the intestinal mucous membrane gives rise to the manifestations of hemorrhoidal disease, which certainly very often depends upon other conditions than the impeded passage of blood through the fatty liver. The excretion of bile is also interfered with in higher grades of fatty liver, for the intra-lobular, capillary, biliary passages are narrowed by the distended liver-cells, and the flow of bile through these passages is impeded. This is particularly shown by the fact that the cells in the central region of the lobule are of a diffuse brownish color, or are filled with numerous yellow granules. The disturbance

can even be noticed by the naked eye, the centre of the lobules being often colored greenish and in marked contrast to the pale yellow marginal portions of the lobules, which are rich in fat. But neither is the escape of bile ever so far obstructed as to result in the absorption of bile and in jaundice. If one now and then comes upon cysts within the fatty liver containing bile, this is doubtless an accidental coincidence, and does not prove that in the fatty liver the interlobular biliary passages are exposed to any considerable pressure.

The supposition that fatty infiltration of a higher grade may not be without its influence on the *amount* of bile secreted, is well founded; for the preparation of bile is bound up with the protoplasm of the liver-cells, and if this suffers a diminution corresponding to the amount of the accumulated fat, then the amount of secretion produced by it might also grow less, the more so as the flow of blood is impeded in a liver overloaded with fat, and this must exert a restricting influence on the activity of the secretion. The above supposition is borne out by the fact that in extreme degrees of fatty liver post-mortem examination shows the gall-bladder empty and the contents of the intestines of a pale, ashen-gray color. It is true that the diminution of the biliary secretion does not, as a rule, make itself distinctly noticeable during life. As we depend entirely upon the coloration of the fæces for our judgment concerning the activity of the biliary secretion, and as this coloration is influenced by other circumstances as well as by the amount of bile poured into the bowels, it is evident that slight variations in the quantity of the biliary secretion must entirely escape our notice, and that we are only able to recognize a very serious diminution in or the entire cessation of the secretion.

The bile secreted by a fatty liver is not to be distinguished in *quality* from that of a healthy liver. On post-mortem examination we find the gall-bladder sometimes filled with a pale and thin secretion, sometimes with one that is dark colored and tenacious, differences which depend on the degree of concentration of the same and the greater or less length of time it has been retained within the bladder, as well as upon the amount of mucus secreted by the mucous membrane of the biliary passages.

These differences are met with in the same way, both in a perfectly healthy state of the liver and in very varied conditions of disease of this organ. There are, it is true, isolated statements according to which it is claimed that the bile originating from a fatty liver contained albumen (Thénard), or was very rich in fat (Lereboullet), or that it possessed a peculiar very offensive smell (Addison), which might have depended on some transitory, stinking fatty acid; but other reliable observers have recognized none of all these changes.

The sugar-producing function of the liver is likewise not arrested by the accumulation of fat, although it is to be supposed that the displacement of the cell-protoplasm through fat, as well as the disturbance in the current of blood, likewise causes a corresponding interference with the formation of sugar (Frerichs, loc. cit., p. 315).

Symptoms.

The symptoms of fatty liver are, in most cases, of a very indefinite kind. The lighter forms give rise to absolutely no characteristic attacks, and can therefore hardly lay claim to the name of a disease. But even in the higher grades the manifestations are not always of a kind to afford us a certain guide to diagnosis.

The most important symptom is the *enlargement in the area of the liver.* As the fatty liver extends itself chiefly in the direction of its flat surface, increasing less in thickness, and as its flabby consistency makes it more disposed than otherwise to settle downward, a comparatively slight increase in volume betrays itself by the extension of the area of liver-dulness. According to the results of percussion, one might suppose the liver to be larger than it actually proves to be on post-mortem examination. The enlarged liver extends a greater or less distance below the ribs, and in high grades of fatty infiltration its anterior border may readily descend as low as the level of the umbilicus. Palpation of the liver is not always practicable, even when this organ is greatly enlarged, either because the abdominal walls are too thick and fat, or because they are too tense.

But when circumstances admit of satisfactory palpation, the liver is felt to be smooth, soft, and of flabby consistency. It is hard to define the edge of the liver by the touch; when we succeed in this it is found to be thickened and rounded off.

In many cases fatty liver, even when it has grown to be very voluminous, causes no *subjective manifestations* whatever, or, at most, the patient has a feeling of fulness and uncomfortable pressure in the region of the liver and stomach, especially on lying upon the left side. In some cases, however, particularly in tuberculous patients, the distress caused by the liver reaches so high a grade, and so greatly crowds into the foreground, that the patient quite forgets his original difficulty, and comes to believe that his main trouble lies in the liver. Even the physician may thereby be misled. If the fatty liver is very rapidly developed, and the serous covering of the same is stretched by the rapid distention of the organ, then more active sensations of pain arise, which, in rare instances, may even become very severe.

Disturbances on the part of the *digestive apparatus* are, it is true, very common in the higher grades of fatty liver; but these cannot by any means always be brought into a causal connection with the fatty liver, being in great part caused by the pathological conditions which lie at the foundation of the same, or by accidental complications. Digestion is disturbed; there is loss of appetite, frequent eructations of gas occur, with distention and sensitiveness of the epigastrium. The action of the bowels is usually sluggish and irregular; as a rule the fæces are normal in color, though, in more advanced cases, where the formation of bile is diminished, they are sometimes found to be pale, clay-colored, or ashen gray. At times a striking tendency to diarrhœa is found associated with fatty liver, profuse and exhausting discharges from the bowels being set up on quite insignificant provocation. Hemorrhages from the rectum, and other so-called hemorrhoidal troubles, are also associated with the higher grades of fatty liver, and might, with more justice than any of the previously mentioned manifestations on the part of the alimentary canal, be considered as depending on the disturbed flow of portal blood through the narrowed capillaries of the fatty liver.

Persons affected with this disease occasionally show a pecu-

liar condition of the *external skin.* The greasy quality of the skin—such as appears in corpulent persons and those addicted to strong drink—has probably no connection with fatty liver, but depends on hypersecretion of the sebaceous follicles, and an unusually large admixture of fat in the secretions of the skin generally, which itself again is the result of overloading of the blood with fatty matter. On the other hand, Addison states that, in fatty liver, he has found the skin to be pale and bloodless, of a waxy transparency, and that it felt smooth and soft as velvet. The skin was sometimes of a pure white, sometimes of a dirty yellowish color, and the change described occurred particularly in the skin of the face, without, however, being absent in other portions of the body. Addison was of the opinion that there could be no doubt among physicians but that this change in the quality of the skin was nothing less than a constant manifestation in fatty liver. But it is a question whether it stands in any intimate relation to fatty liver. It is true that consumptive women, in whom we meet with a fatty liver oftener than we miss it, not rarely show this alteration of the skin; we admire their fine and delicate complexion, but they owe this not to their fatty liver, but to their hectic condition, perhaps also to the profuse sweats with which phthisical patients are affected.

Diagnosis.

In the entire absence of other symptoms, especially of functional disturbances, it is impossible to arrive at the diagnosis of the milder grades of fatty liver which have not yet led to any noticeable enlargement of the organ. But as soon as the increase in the size of the liver by the accumulation of fat has become demonstrable by percussion, the diagnosis, as a rule, presents no difficulties, provided that proper weight is given to the etiological conditions which, according to experience, lie at the foundation of fatty liver. If we find a distinctly enlarged liver, which feels smooth and soft, while at the same time there is no enlargement of the spleen, no ascites, no icterus, and if we find these conditions in a stout person of gluttonous habits, or in a habitual drinker, in a consumptive or otherwise cachectic person, we

shall not go far amiss in assuming the presence of a fatty liver. The diagnosis will be still further confirmed if, at the same time, we find evidences of abdominal plethora, such as disturbances of digestion, distention of the region of the stomach, frequent eructations of gas, irregular, sluggish action of the bowels, hemorrhoidal troubles, etc. It is evident that in persons who present the above-mentioned etiological conditions, in whose case we may, therefore, presume the existence of fatty liver, we are not justified in concluding that this condition does not exist because of the lack of any increase in volume on the part of the liver. In cases of pulmonary tuberculosis, and of other chronic maladies associated with cachexia, we are more likely to be involved in doubt as to whether the notably enlarged organ represents a fatty or an amyloid liver. Here the decision depends on the consistency of the tumor, for the amyloid liver feels hard and resisting, and its margins can generally be easily defined by the touch, while the fatty liver, if it can be palpated at all, feels soft, and its margins are difficult to follow. If the consistency of the organ cannot be determined, then the existence of a firm tumor of the spleen, the presence of albumen in the urine, of ascites, and of dropsical swelling of the lower extremities would be evidence in favor of amyloid liver, and the absence of all these signs more in favor of fatty liver; for other diseases associated with enlargement of the liver would generally be excluded by the external circumstances of the case, or by the absence of certain definite symptoms belonging to them.

Duration, Termination, Prognosis.

We do not propose here to take into account those comparatively rare instances of acute fatty changes in the liver in acute phosphorus-poisoning, and in the so-called acute fatty degeneration of new-born babes and of puerperal women, which, as a general rule, terminates fatally within a few days. Ordinary fatty liver is a chronic malady, which may end in a return to the normal condition, after having lasted at least for a few months, and often for years, or which may continue in about the same degree to the end of life. In the latter case, it is true, the fatty

liver, to a certain degree, causes a disturbing reaction on the general organism by diminishing the production of bile, and by the accompanying disturbances of digestion; but no influence can be attributed to it tending directly to shorten life. The prognosis of fatty liver is therefore good, at least so far as life is concerned. There can be no doubt that fatty liver is curable, and that the fat accumulated therein is very often entirely absorbed. But whether this is to take place in any individual case depends upon whether the causes of the fatty liver are of a temporary or permanent character, or whether or not they are removable.

Therapeutics.

In the treatment of fatty liver the most careful attention must be given to ascertaining the causes which lie at the foundation of the same, for as soon as the supply of fat to the liver is cut off, or the development of fat in the liver-cells ceases, we may confidently look for the gradual disappearance of the fat already accumulated in the organ. This end, it is true, can only be attained in those cases in which the fatty liver is the result of an unwise diet, of a luxurious and inactive method of life, or where it depends on an excessive indulgence in alcohol, for there can scarcely ever be any hope of removing the causes of fatty liver in consumptives and other cachectic subjects. In cases of the first variety the regulation of the dietetic conditions alone is often sufficient to re-establish the normal state of things. The diet must here be limited to the necessary amount; it must be made as poor as possible in fats and in such matters as have been found by experience to favor the development of fat in the organism. All fats and fatty varieties of meat are to be avoided; indulgence in starchy and sweet dishes is also to be reduced as far as possible. On the other hand, lean varieties of meat are to be recommended, especially the meat of fishes, as well as fresh fruit and green vegetables. Alcoholic drinks are to be forbidden, especially also heavy beer and strong, sweet wines; the patient is to be restricted to a glass of light, astringent, red wine, and is to be encouraged to drink a good deal of water. The patient must not sleep too long, and must especially avoid

sleep after his principal meal; he must rise early, indulge in active exercise in the open air, and likewise secure appropriate mental occupation.

If we are dealing with individuals in whom we have reason to believe that besides the fatty liver there is also fatty degeneration of the muscle of the heart, then the *régime* just recommended must not be introduced too suddenly, and its operation must be carefully watched in order to avoid all dangerous accidents on the part of the heart. The withdrawal of the stimulating effect of alcohol, in particular, to which the heart has once become accustomed, might seriously react upon the activity of this organ.

The action of dietetic regulations is sought to be aided by medicinal means. The alkalies, in particular, are employed in fatty liver, because, according to the current doctrine, they saponify the free fat, and thus render it fit for absorption. The alkaline and saline mineral waters are the means most extensively used in the treatment of fatty liver, especially the springs of Carlsbad, Marienbad (Kreuzbrunnen), Vichy, Ems, Kissingen, Homburg, etc. When we are dealing with anæmic persons, for instance with women who, in addition to a strong tendency to the formation of fat, suffer from amenorrhœa and kindred disturbances of menstruation, preparations of iron and the chalybeate mineral springs of Spa, Pyrmont, Schwalbach, etc., give excellent results. Similar results to those following the use of mineral waters, although less active, are obtained by the "herb cures" and "fruit cures" sometimes undertaken, which are, accordingly, better adapted to weakly and reduced individuals.

The difficulties of digestion which so often exist in fatty liver are treated with good results by means of bitter vegetable substances, gentian, taraxacum, chiccory, and the like. If there is great torpidity of the bowels, aloes, colocynth, and other drastics must be employed; while, on the other hand, a tendency to diarrhœa is to be met by astringents.

In the fatty liver occurring in pulmonary consumption and other chronic maladies, no direct treatment can generally be carried out. In the less advanced cases of pulmonary tuberculosis, the alkaline mineral waters containing carbonic acid, such

as those of Ems, Selters, Obersalzbrunn, Gleichenberg, etc., are to be recommended as acting favorably, not only against the tuberculosis, but also against the fatty liver. The pains over the region of the liver which sometimes occur in patients of this kind are to be combated with mustard-plasters, or even, in case of need, with a hypodermic injection of morphine. The fatty liver of consumptives will have to be regarded as furnishing a contra-indication to the use of cod-liver oil and other fatty matters (milk).

PIGMENT LIVER. MELANÆMIC LIVER.[1]

Literature.

Frerichs, Klinik der Leberkrankheiten. I. 1858, p. 325; also Atlas, Plates IX. and X.; the representations referred to are in part also reproduced in Lebert's Atlas of Pathological Anatomy.—*Heschl*, Zeitschr. d. Gesellsch. d. Aerzte in Wien. 1850.—*Planer*, Ibid. 1854.—*Arnstein*, Bemerkungen über Melanæmie und Melanose. Virch. Arch. LXI., p. 494; also, the same, LXXI., p. 256.—*Mosler*, Ueber das Vorkommen von Melanæmie. Virch. Arch. LXIX., p. 369.—*Kelsch*, Contribution à l'anatomie patholog. des maladies palustres endémiques. Arch. de physiologie norm. et patholog. 2 Sér. Tome II., p. 690. 1875.

Abnormal pigmentation of the liver is of very common occurrence. Aside from the yellow, brown, or greenish coloration, involving all the tissues of the liver, which accompanies icterus from obstruction, and usually disappears with the subsidence of the same, there are two conditions, in particular, that belong under this heading, viz., the *rusty-brown atrophic liver* and the *melanæmic liver*. So far as the first is concerned, the lively rusty-brown color thereof depends on the fact that the shrivelled liver-cells enclose numerous brownish red granules, sometimes regular pigment-balls, which are generally supposed to consist of excreted biliary coloring matter. The function of the liver does not seem to be seriously influenced by this condition, which, in fact, gives no symptom of its existence during life, and is only accidentally discovered at the post-mortem table.

[1] As melanæmia has been treated of in connection with diseases of the spleen (this Cyclopædia, Vol. VIII.), we shall here confine ourselves to setting forth the part which the liver takes in this disease. With regard to the literature of the subject, reference may be had to the section just named.

The condition of things is different in the pigment liver, κατ' ἐξοχήν, or the melanæmic liver. This owes its origin to a peculiar alteration of the blood, which is designated melanæmia, "black blood." The pigment here lies principally in the interior of the blood-vessels of the liver, in part also outside of the same, in the interstitial connective tissue, while the parenchymal cells of the organ remain quite free. The amount of pigment-matter accumulated in the capillaries is in some cases so considerable that serious disturbances are caused in the blood-stream, followed by an array of symptoms dependent thereon. This form of pigment liver consequently asserts itself as an actual disease.

The essential character of melanæmia depends upon the fact that abundant quantities of black pigment-matter in solid form are intermingled with the blood. The pigment appears partly in the form of fine, roundish granules, which show a tendency to unite into larger masses, and partly in the form of coarser flakes and clods. This originally exists in a free form in the blood—that is to say, the pigment-granules are not enclosed in cells, but float free in the blood-plasma. But the main portion of originally free pigment appears, soon after its development, to be taken up by the colorless blood-corpuscles. The latter thus become pigment-carrying cells. When they leave the blood-vessels, wandering from the same, the pigment, of course, also passes with them into the tissue surrounding the vessels, where it may remain deposited for a long time.

The cause of melanæmia lies in the malignant forms of malarial fever. According to the more recent investigations of Arnstein and Kelsch, it appears as though, with every paroxysm of fever, a large number of red blood-corpuscles were destroyed. The coloring matter thus set free separates in solid form, and circulates with the blood. In well-developed forms of melanæmia, during a period shortly following an attack of intermittent fever, pigment is to be found wherever the blood goes. At a later period the pigment-carrying cells are confined to certain vascular areas, and the greater part, if not the entire mass of the pigment, disappears from the general circulation.

No definite conclusions have yet been reached on the question of where the destruction of red corpuscles and the formation of

pigment take place,—whether the latter is confined to certain organs; nor on the question, so intimately connected with this, concerning the relations of melanæmia to melanosis—that is, to the depositing of black pigment in certain organs. Frerichs and Virchow advocate the view that the formation of pigment is principally connected with the spleen; that from here the pigment passes into the splenic and the portal veins; that a portion thereof is retained in the capillaries of the liver, while the remainder passes through the liver and goes the round of the general circulation with the blood. According to this doctrine melanosis of the spleen would be the primary change, while melanæmia would be a secondary manifestation. Arnstein and Kelsch maintain the opposite view; they regard melanæmia as the primary change, and in melanosis of the spleen, the liver, the spinal cord, etc., they behold a secondary alteration dependent on the former. They believe that the disintegration of red corpuscles and the separation of pigment take place everywhere within the interior of the blood-vessels, but that the pigment circulates with the blood but a short time—a few hours, or at the most a few days; in fact, that the melanæmia very soon disappears, because the pigment is—that is, the pigment-carrying cells are—restricted within certain vascular areas, thus causing the melanosis or black coloration of the parts concerned. The stream of pigment-carrying cells stagnates in the capillaries and veins of those organs in which the rapidity of the current is very slight, especially in the liver, the spleen, and the spinal cord. But while in the spleen and the spinal cord the pigment-carrying cells pass out of the vessels into the tissues of those organs, they are long retained within the capillaries of the liver. It may be asserted, in general, that so far as concerns its extension and deposition in individual organs melanæmic pigment behaves in a manner quite analogous to that of granular coloring matters which have been artificially introduced into the blood.[1]

It has been settled by numerous observations, and, of late,

[1] Compare *Ponfick*, Studien über die Schicksale körniger Farbstoffe im Organismus. Virch. Arch. XLVIII., p. 1. *Hoffmann* und *Langerhans*, Ueber den Verbleib u. s. w. des Zinnobers. Ibid., p. 304.

particularly by those of Kelsch (loc. cit., p. 724), that the main source of pigment-matter in melanæmia is to be found in the blood of the splenic vein and the portal vein, especially in the hepatic branches thereof. The blood of these vessels is incomparably more rich in pigment than that at any other point in the vascular system. The colorless corpuscles which carry pigment are also found much more abundantly supplied therewith in the vessels above named than in those which are more peripheral. These cells are stuffed quite full of pigment, and look more like accumulations of pigment than true cells.

The *anatomical conditions* of the liver in melanæmia differ according to the stage and the duration of the disease. In recent cases one finds the liver normal in size or a little enlarged, very rich in blood, tender and friable, and of a peculiar dusky, dirty brown color. After the disease has lasted for some time the hyperæmic swelling of the liver is lost, the organ shows a color resembling that of chocolate, steel gray, or dark slate-colored. This coloration is either uniform, or the brownish lobules are seen surrounded by a black border, the latter taking place when the pigment is principally accumulated in the interlobular veins. Interstitial hepatitis is very often developed in the course of melanæmia. The interlobular connective tissue then forms broad fibrous bands, thickly infiltrated with small round cells, the lobules grow smaller, the entire organ shrivels and presents the peculiarities of granular liver, although with this difference, that the fibrous intermediate tissue is colored slate gray or blackish, while atrophied hepatic lobules show a pale color.

Microscopic examination of the melanæmic liver shows that the liver-cells are sometimes overloaded with fat-drops, still more frequently are impregnated with an unusually abundant quantity of biliary coloring-matter, but that they never enclose the slightest trace of melanæmic pigment. The latter is to be found almost exclusively in the interior of the blood-vessels, especially in the capillaries of the hepatic lobules. The pigment is not found free, or only to a very small extent, but rather incorporated in the leucocytes, and the capillaries are more or less completely stuffed with such pigment-carrying cells. Toward the central vein of the lobule the capillaries are sometimes visibly distended, the

liver-cells lying between them being thus compressed and falling a prey to atrophy, in the same manner as may be observed in the engorged liver of persons with cardiac disease. The centre of the hepatic lobules is sometimes so altered that nothing is to be seen but the enormously distended capillaries, stuffed with large pigment-carrying cells, and only bounded by narrow fibrous bands (the remnants of the framework of atrophied liver-cells). But the *capillaries* of the lobules are not the only vessels containing pigment, which is sometimes uniformly distributed over the entire lobule, sometimes more heaped up at certain points, for pigment is also to be found in the central vein of the lobules as well as further on in the hepatic veins. It is especially liable, at times, to be accumulated in large quantities in the interlobular branches of the portal vein, as well as in the small branches of the hepatic artery, which are distributed to the interlobular connective tissue, so that the lobules are seen to be surrounded with a blackish belt. A certain portion of the pigment afterward also appears outside of the vessels, especially in the interlobular connective tissue. This probably comes about through the development of an inflammatory disturbance, an interstitial hepatitis, during which the pigment-carrying leucocytes emigrate and locate themselves in the fibrous tissue surrounding the vessels.

In those persons who succumbed to an attack of fever and presented intense melanæmia, Kelsch found the liver saturated with bile, the gall-bladder enormously distended, and the intestines flooded with bile. The biliary passages were always found free. This regular coincidence of polycholia and melanosis of the liver in malignant marsh-fevers appears to be more than a mere accident.

Although in all fatal cases of melanæmia the liver is found more or less rich in pigment, and although the presumption seems justified that the same condition exists in the cases that do not terminate fatally, still this alteration in the liver by no means makes itself known in all cases of melanæmia through definite symptoms on the part of the liver and in the domain of the portal vein. In fact, cases of melanæmia with prominent involvement of the liver and the gastro-intestinal canal are more rare than those in which the brain-symptoms occupy the fore-

ground. Among the 51 cases of melanæmia observed by Frerichs in Breslau, 38 of which ended fatally, severe cerebral symptoms occurred 28 times, albuminuria 20 times; cases of profuse diarrhœa, on the other hand, 17 times (5 of which were dysentery). Severe intestinal hemorrhages occurred 3 times; icterus was present in 11 cases, although not in a very marked degree. In all the cases that resulted fatally the liver showed itself rich in pigment; in 10 of these it was enlarged and rich in blood; in 8 it was atrophied; in 9 the liver-cells were rich in fat; lardaceous matter was found 3 times, although only to a limited degree.

According to Frerichs, the fact of the liver being involved in melanæmia in some cases makes itself known by a feeling of pressure in the right hypochondrium, as well as by an increase in the size of the liver. At the same time, these manifestations may fail even when the capillaries of the liver are stuffed full of pigment. A slight icteric discoloration of the skin and of the conjunctiva, as well as the presence of biliary coloring matter in the urine, is often to be found, although this symptom, too, is anything but constant. The abundant secretion of bile, which seems to be the rule, especially in more recent cases, cannot be recognized in the living subject, and cannot be utilized as a symptom any more than the presence of albumen in the bile, which has been established by Frerichs. If the flow of portal blood through the liver is, to a considerable degree, disturbed, in consequence of the obstruction of the vessels with pigment-carrying cells, then there is stagnation of the blood-stream in the roots of the portal vein, which betrays itself on the mucous membrane of the intestinal canal by profuse diarrhœa, or even by hemorrhage into the intestine. A serous exudation into the cavity of the peritoneum has also sometimes been seen to arise, under these circumstances, in an acute manner. It must be admitted that it is not yet determined beyond all question whether all these manifestations may be referred directly to the obstruction of the blood-passages in the liver; for the alterations in the liver have also been found in those cases where there was no diarrhœa, hemorrhage, or similar manifestation, and the hemorrhages which Frerichs observed in three cases arose in a distinctly intermittent manner, and gave way to quinine, while

they resisted treatment addressed directly to hemorrhage. It is difficult to reconcile the intermittent character of the manifestations—that is, the hemorrhages—with the supposed cause, viz., the obstruction of the vessels of the liver. The diarrhœa existing in the cases reported by Frerichs might also be suspected of owing its origin to other causes than to the impermeability of the vessels of the liver, and the consequent condition of stagnation in the portal vein. At all events, the author distinctly calls attention to the simultaneous occurrence of dysentery at the time of the endemic described by him. In some cases of melanæmia the alterations which the liver has suffered only make themselves manifest from the period of time when atrophy of the organ sets in.

The fixed points in the diagnosis of pigment liver are, accordingly, few in number and insecure. But the task of the physician is not limited to making a diagnosis of the pigment liver which may exist; he must rather turn his attention to the general condition of the patient—that is, to the melanæmia in all its manifestations. The diagnosis of melanæmia depends partly on the demonstration of the previous existence of malarial infection, partly on the direct microscopic examination of the blood in which the black pigment is to be sought, and partly, at last, on the manifestations on the part of the spleen, the brain, the urinary secretion, and the external skin which belong to melanæmia. When we have in this way arrived at the diagnosis of melanæmia, we shall be justified in referring the above-described symptoms on the part of the liver and the gastro-intestinal catarrh to the existence of pigment liver; but the diagnosis of pigment liver could not be sustained without due reference to those more remote conditions.

If the views maintained by Arnstein and Kelsch with regard to the pathogenesis of melanæmia are correct, the *development* of pigment liver would have to be an acute process, inasmuch as the pigment-matter rapidly developed during the fever-paroxysms is arrested in the vessels of the liver. But, when once pigment liver is developed, this condition remains pretty nearly stationary for a considerable time. After the cessation of the attacks of fever, however, the pigment does also seem gradually

to disappear again from the vessels of the liver. At the same time, the return of the liver to its normal condition is exceptional, the rule being that inflammatory proliferation of the interstitial connective tissue, atrophy of the parenchyma of the liver, and cirrhotic shrivelling of the entire organ follow. The *prognosis*, therefore, aside from the other dangers of melanæmia, must always be regarded as unfavorable, or at least doubtful, even with reference to the liver.

The task of *therapeutics*, over against pigment liver, consists, above all else, in the duty of removing the attacks of intermittent fever, for with every attack the amount of pigment is increased, and the impermeability of the blood-vessels of the liver is heightened. Quinine, used in appropriately large doses, is here the almost sovereign remedy. Not only is the fever thereby cut short, but the intermittent hemorrhages and the acute ascites which follow immediately upon the more extensive capillary obstructions within the liver are most successfully combated by quinine. After the cessation of the fever paroxysms, the treatment may be directed toward the remaining local disturbances of the liver and of the other organs involved. The hyperæmia of the liver generally disappears of itself with the cessation of the fever. There is no means of prevention to be directed against the gradually developing atrophy of the liver. The symptoms dependent on shrinking of the liver, such as chronic gastric catarrh, profuse diarrhœa, or ascites, must be met on the general principles appropriate in each case. The same is true with regard to the conditions of fatty and amyloid infiltration of the liver, which are sometimes developed after long-continued malarial fevers.

THE

PARASITES OF THE LIVER.

HELLER.

PARASITES OF THE LIVER.

General Observations.

THE number of parasites thus far found in the liver in man is but small. The list is completed on the mention of the echinococcus, cysticercus, pentastomum denticulatum, and, finally, the so-called psorosperms.

The only one of these which up to the present time is of any practical consequence is the echinococcus. The rest are, in part, but rare visitors, nor are there any signs known at present which might be produced by their presence.

Echinococcus.

Heller, This Cyclopædia, Vol. III., pp. 557 to 594.—*Neisser*, Die Echinococcen-Krankheit. Berlin, 1877.—*Davaine*, Traité des Entozoaires. 2. éd. Paris, 1878.—*Kuechenmeister* u. *Zuern*, Die Parasiten des Menschen. 2. Aufl., 1. Lief. Leipzig, 1878.—*Leuckart*, Parasiten. 1. Bd.

The natural history and general pathology and therapeutics of echinococcus, as well as those, in particular, of liver-echinococcus, have already been so fully treated of in Volume III. of this Cyclopædia that we should not be justified in again entering upon them at any length. It will be sufficient to call attention to the main points, and to mention any new observations or advances that may have been made, especially in the line of therapeutics.

The echinococcus usually occurs in the liver singly, it being more rare to find several specimens present. By its growth it not only crowds the liver-tissue aside, but also causes it to

undergo extensive atrophy. It appears as a circumscribed tumor, showing itself early when situated on the surface, later when situated more deeply, and stands out farther above the surface as it increases in size. Its growth is very slow, years seeming to be required before it attains any considerable size. In very many instances the echinococcus dies of itself, without any demonstrable cause, and undergoes retrograde metamorphosis, so that finally nothing remains but a cheesy or chalky collection enclosed in a capsule of connective tissue, and sometimes containing remnants of the membrane, hooklets, or even calcified tapeworm heads. If it does not die, it gradually attains a very considerable size.

The cause of echinococcus varies according to its situation in the liver. When developed upon the upper surface of the liver, it displaces the thoracic viscera upward, while the liver itself is pushed downward. When situated upon the surface of the right lobe, in particular, it pushes the diaphragm before it, either with or without perforation of the same, crowds the lung to the left, and rises so high that the right side of the chest seems chiefly filled therewith; the heart is displaced to the left. The relation of things is of course somewhat changed when there is a previous adhesion of the two pleural surfaces to each other. An echinococcus which has risen into the pleural cavity may break through the lung into the air-passages, or evacuate itself externally through the thoracic walls,[1] provided it has not previously induced death by dyspnœa or marasmus.

The following case from Bartels' clinic may here be briefly reported as an illustration of echinococci thus mounting upward, inasmuch as, like so many cases going to make up the Annual Reports on the Progress of Medicine and Surgery, this has not yet found a place in the literature of the subject.[2]

A well-nourished girl, twenty-two years of age, had suffered for three years with increasing thoracic troubles, especially dyspnœa, and for a year and a half with severe pains under the right shoulder-blade. On admission, in October, 1868, the right half of the chest was enormously distended, the intercostal spaces on that side very much widened, with lateral curvature of the spine. Resonance on percussion

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[1] *Hertz*, This Cyclopædia. Vol. V., p. 467.

[2] *Deutsch*, Ein Fall von Echinococcusblasen im Pleurasack durch die Operation zur Heilung gebracht. Dissert. Kiel, 1869.

was entirely lost on the right side, the dulness extending as much as an inch beyond the left border of the sternum, excepting that there was a tympanitic resonance over the second costal cartilage of the right side, the pitch of which changed on opening or shutting the mouth. The apex beat of the heart was found in the axillary line, at first in the sixth, afterward in the seventh intercostal space. The area of liver-dulness hardly passed below the arch of the ribs, but spread gradually downward. No fever. In January, 1869, the right pleural cavity was opened into by an operation in the sixth intercostal space. About 5,000 c.ctm. of fluid were evacuated with some 300 large and small echinococcus cysts. The cavity was syringed out several times a day with a one per cent. solution of common salt, which brought away many more cysts. There was long-continued suppuration, with fever. Gradual diminution of the size of the cavity followed, partly by the demonstrable unfolding of the right lung, partly by the rise of the liver to its normal position, and partly through a slight contraction of the chest-wall. The state of the general nutrition was admirable.

The healing process was very gradually completed, until but a narrow fistula remained. The patient died four years[1] after the operation. On post-mortem examination the right lobe of the liver was found remarkably diminished in size, reduced to about the usual size of the left lobe, while the latter was greatly enlarged, about as large as a normal right lobe. The surface of the right lobe was very firmly bound to the diaphragm, and to a moderate area of the base of the right lung, by hard, cicatrized masses of connective tissue, disseminated with little chalky concretions, by means of which the continuity of the diaphragm was interrupted. A fistulous track, surrounded with callous, slaty tissue, the remains of the opening made by the operation, led through the chest-wall to this cicatricial tissue.

So far as I can ascertain, this is the only case, aside from one mentioned by Frerichs,[2] in which vicarious hypertrophy of the rest of the liver-tissue has been observed, similar to what took place in a case previously described by me, after probable traumatic destruction of a part of the right lobe of the liver.[3] In the kidneys such vicarious hypertrophy is not so very rare.

The results of echinococcus, when it extends downward, make themselves felt, above all, in the organs there found containing or consisting of cavities. Compression of the biliary passages is followed by obstruction of bile and icterus; compression of the ascending vena cava or of the portal vein leads to disturbances of circulation and their results.

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[1] *Neisser* has, evidently by mistake, spoken of this case as having died four days after the operation, whereas it was four years before a post-mortem was rendered possible.

[2] Klinik der Leberkrankheiten. II., p. 223.

[3] *Heller*, Virchow's Archiv. 51, p. 355. 1870.

Rupture into the inferior vena cava causes immediate death, by embolism of the pulmonary artery. Rupture into the abdominal cavity is usually followed by fatal peritonitis; occasionally temporary recovery occurs. An opening into the biliary passages may lead to complete recovery, temporary icterus being caused by the obstruction of bile through the cysts that are passing through.

A case of this kind was recently reported from Nothnagel's clinic.[1]

In the course of several years a tumor in the upper abdominal region appeared repeatedly, and disappeared again in a short time, with severe pain. During the last attacks icterus arose. Cysts were evacuated from the bowels, about four hundred being counted in the clinic.[2]

Acute inflammatory manifestations are not usually seen in echinococcus, except as the result of external influences. Whereas, as a rule, echinococcus causes no rise in temperature, yet under these circumstances there may be severe fever, with active suppuration, around the echinococcus. Extensive abscess-formation in the liver may cause death.

The other form of echinococcus, the *multilocular*, shows some differences from the ordinary form. Most prominent among these is the almost uniform occurrence of icterus and of swelling of the spleen, while ordinary echinococcus only shows the former when it presses on the biliary passages, or when, breaking into them, it causes their temporary closure by the passage of cysts.

Among 40 cases of echinococcus multilocularis, the condition of the spleen is mentioned 29 times; in 25 of these there was a tumor of the spleen. In 33 cases the question of icterus is reported on; in 28 of these it was present. Tumor of the spleen was absent but four times; icterus but 5 times; in one of the latter cases, however, it seems to have existed before.

Of late years a number of new cases of this rarer form have again been made public. Klebs[3] has collected 21 cases (25, including the doubtful cases of Dittrich and Meyer and Scheuthauer's second case, which does not belong here); Prouge-

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[1] *Westerdyk*, Berl. klin. Wochenschr. 1877, p. 629. No. 43.

[2] Compare *Barth*, Arch. d. Heilkunde. 13. 187. (This Cyclopædia. Vol. III., p. 590.)

[3] Patholog. Anatomie. I., p. 517.

anski [1] in 1873 had collected 17 (19, with two that had not yet arrived at a post-mortem); Morin [2] mentions 32; and in 1876 I was able to count up 35 cases in the human subject. To these may now be added the following five new ones:

36. Reported by Laudenberger.[3] A man, thirty-four years old, an Italian, had icterus and a tumor of the spleen. In the right lobe there was an ichorous cavity as large as a fist, on the lower surface of which there were connective-tissue masses disseminated with cysts. In the portal fissure, the lymphatic vessels were filled with the same; so were likewise the lymphatic vessels and finer biliary passages toward the sharp border of the left lobe. In the subserous cellular tissue of the abdominal walls over the navel were some hard, whitish yellow nodules, of the size of a nut, connected with the right lobe of the liver by connective tissue, which likewise proved to be multilocular echinococci.

37. Reported by Dean.[4] A blacksmith from Schwangau, in Bavaria. Thirty-nine years of age; icterus; spleen normal; dropsy. Liver twice its natural size; weighs ten pounds; surface shows nodules resembling cartilage, with glutinous contents; in the right lobe a cavity as large as a head, with bloody, serous, glutinous contents mixed with crumbled fragments of tissue.

38. Reported by Dean (ibid.). An echinococcus multilocularis of the size of a goose egg in the liver of a negro woman.

39. Reported by Scheuthauer.[5] A servant-girl from Kärnten, thirty years of age. Icterus. Spleen greatly enlarged. In the right lobe of the liver two masses, each of the size of a goose egg, one at the anterior, the other at the posterior border, as hard as cartilage, and disseminated with mucilaginous granules, varying in size from that of a poppy-seed to that of a pea; in the middle a cavity filled with whey-like fluid. A third node was found in the portal fissure, from which arose three thickened lymphatic vessels filled with mucilaginous granules; a node of the size of a plum in the left longitudinal fossa, one of the size of a bean at the right border of the liver.

40. Reported by Kuechenmeister.[6] A merchant, thirty-two years old, the son of a butcher, from Bavaria. Icterus. An echinococcus multilocularis of the size of a fist in the right lobe of the liver.

Diagnosis.

The diagnosis of echinococcus of the liver is at first very difficult, if, indeed, possible. It is only during its further growth

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[1] Dissert. Inaug. Zurich, 1873.

[2] Dissert. Inaug. Bern, 1876.

[3] Würtemb. Correspondenzbl. 1875, p. 198. No. 45.

[4] St. Louis Med. and Surg. Journal. 14, p. 420. 1877

[5] Wien. allgem. med. Zeitung. 1877. Nos. 21 and 22.

[6] Parasiten des Menschen. I., p. 192. 1878.

that a more or less certain diagnosis can be made. If, in a comparatively young person, a marked swelling in the region of the liver comes on slowly and gradually, without fever or any considerable pain, without any marked disturbances of nutrition or cachexia, and if the tumor gives evidence of fluctuation, we may think of echinococcus. The probabilities may be increased by the exclusion of other varieties of tumor. The affections to be considered under the head of differential diagnosis are chronic abscess of the liver, aneurism, dilatation of the biliary passages, hydronephrosis, cystic kidney, and in women ovarian cysts. Other fluctuating tumors, such as hæmatometra, enormous dilatation of the urinary bladder, cystic dilatation of the remnants of the urachus, are altogether too rare, and are also hardly liable to remain unrecognized on anything like a careful examination. Neither is the pregnant uterus likely to be a source of error.

It is far more difficult, on the other hand, to distinguish an echinococcus arising from the upper surface of the liver from a pleuritic exudation. For even the sign insisted on by Frerichs[1] as well as Bartels,[2] that in echinococcus the line of dulness at the back descends as it approaches the spine, has been shown by more recent observation[3] not always to hold good.

I should like to call attention to one manifestation, for the sake of having it further observed. Traube, in his clinic, pointed out pain in the right scapula as characteristic of disease of the liver, so that where this symptom is present a pleuritic exudation might perhaps be excluded. These same pains were present in the above reported case of Bartels (p. 484).

All ordinary means for the recognition of this difficulty often leave us in the lurch. An exploratory puncture is the only means which almost invariably gives us a positive conclusion in non-inflamed echinococci, although even here there are some possibilities of error. The exploratory puncture may result in the evacuation of fluid only. If the fluid is clear, of a specific gravity of 1007 to 1015, free from albumen, with an abundant amount of chloride of sodium, six parts per thousand and over,

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[1] Loc. cit. [2] This Cyclopædia, Vol. III.

[3] *Seligsohn*, Berlin. klin. Wochenschr. 1876. Nrs. 9 und 10.

the diagnosis is almost positive; the only other similar fluids which also prove to be free from albumen are the contents of those rare cysts of the broad ligament, and very unfrequently ascitic fluid in persons who are hydræmic as the result of amyloid degeneration, but these are generally of lower specific gravity. The presence of succinic acid or of grape sugar argues in favor of echinococcus.

In looking up the question of the chemical composition of fluids obtained by puncture, Westphal's work [1] will be found of special value. In addition to his own investigations he also gives an outline of the material on hand to date.

The absence of albumen in non-inflamed echinococci is especially to be emphasized in contrast to the confusion which Kuechenmeister [2] threatens to introduce by an utterly incomprehensible mistake. He says: "Very great diagnostic value is attached to the *chemical* examination of fluids obtained by an exploratory puncture. The presence of albumen (demonstrated by boiling, alcohol, or nitric acid), of inosite, or succinic acid, is accepted to-day as the best evidence that a fluid, as clear as water, without scolices or hooklets, nevertheless belongs to echinococci." Older and more recent investigators have unanimously found the *fresh* echinococcus fluid free from albumen. Jacobsen [3] found only a substance resembling casein, which appeared in small quantity on evaporation.

Some statements that have been made with regard to the presence of a small or a large amount of albumen in echinococcus fluids may be credited to the admixture of a transudation fluid.

The diagnosis is unequivocal whenever the microscope shows the presence of tapeworm heads in the sediment, or pieces of echinococcus-membrane are withdrawn; the latter show the characteristic lamination.

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[1] Beitrag zur Lehre von der Probepunktion. Archiv f. Gynäkologie, VIII., p. 1.

[2] *Kuechenmeister* und *Zuern*, Die Parasiten des Menschen, 2. Aufl., I., p. 185, 1878. Aside from an abundant sprinkling of typographical errors, this work is unfortunately otherwise distinguished by numerous errors.

[3] We are indebted for these careful analyses to Prof. Jacobsen, of Rostock, formerly of Kiel—not to "Jacobson," as Neisser persists in calling him.

An exploratory puncture fails to be of any value, so far as a chemical examination is concerned, as soon as inflammation has set in; usually also whenever a previous puncture has already been made.

Mistakes may arise whenever pus or ascitic fluid becomes mingled with the echinococcus fluid, on the withdrawal of the trocar.

But, if suppuration has already arisen, further operative interference is indicated anyhow, whether the abscess is to be referred to echinococcus or to some other cause.

The diagnosis of echinococcus multilocularis meets with other difficulties. As this condition but rarely shows any considerable fluctuation, but is distinguished by its hardness and rigidity, it may be confounded with other kinds of tumors of the liver.

It is to be distinguished from ordinary echinococcus by its almost always being accompanied by swelling of the spleen, generally by the early appearance of icterus, and by the very hard quality of the tumor, if it is accessible to the touch.

Echinococcus is distinguished from cancer of the liver by the much slower course of the former. Cancer always causes general disturbances of nutrition much earlier. Swelling of the spleen is found only in cancer that runs a very rapid course; quick growth excludes echinococcus. When the liver projects under the border of the ribs, cancer-nodules can be felt. Cancer of the liver principally affects persons of maturer years; echinococcus those of a younger age.

Amyloid liver and the hypertrophic form of cirrhosis of the liver are distinguished by the uniform enlargement of the organ. They also cause entirely different manifestations, being, in particular, without the painfulness which is so very frequently present in multilocular echinococcus.

Syphilis of the liver could hardly be confounded with this affection.

Prognosis.

In every case of liver-echinococcus which is still growing, or which is engaged in suppuration, the prognosis must be very guarded, for the result depends on so many circumstances—on

its size, seat, the strength of the individual, etc. The prognosis of the multilocular form is thus far very bad.

Therapeutics.

The most important maxim in therapeutics is that enunciated by Kussmaul,[1] viz., not to wait, in a case of growing echinococcus of internal organs, until symptoms appear which threaten life. A growing echinococcus is a constantly threatening, immediate danger. Furthermore, the healing process takes place more readily in early operations than when longer duration has rendered the enclosing cyst-wall more rigid, and when the change in other organs has been increased by the pressure of the growing parasite.

So far as direct treatment is concerned, the prospect of accomplishing anything by either internal or external medication is extremely slight. Operative measures are the only ones that can be seriously taken into consideration. These divide themselves into two principal groups:

1. Methods by which the parasite is to be made to shrivel and perish. Under this head come simple puncture with a fine trocar, puncture with aspiration, puncture with subsequent injection of iodine, and, finally, electrolysis. The latter seems to coincide in its method of operation with simple puncture by means of a fine trocar. Both these methods can show a number of good results, while the other two have been less successful.

2. The second group embraces those methods which contemplate the opening and the emptying of the sack. The number of methods, with greater or less variations, is large. The first aim of all of them is to bring about an adhesion of the cyst-wall with the abdominal wall, be it by cauterization, or by the introduction of needles, or by thrusting in one or several trocars. A large opening subsequently made permits the emptying of the cyst and its after-treatment until recovery.

Simon's[2] method appears to be the most promising. He

[1] Berlin. klin. Wochenschrift. 1867, p. 545.

[2] Die Echinococcencysten der Nieren und des perirenalen Bindegewebes. Herausgegeben von Dr. H. Braun. Stuttgart, 1877.

recommends multiple puncturing of the echinococcus. The first puncture is to be utilized for confirming the diagnosis by the immediate examination of from forty to sixty cubic centimetres of the contents. If the chemical and microscopic examination confirms the diagnosis of echinococcus, then three more trocars are immediately introduced at sufficient distances apart (at least five ctm.). The trocars are left in position until fluid trickles out alongside of the canulas. An amount similar to what was removed at the first puncture is withdrawn through the canulas daily. Suppuration generally begins on the fourth or fifth day. If the symptoms of general reaction are but slight, we may wait a few days more; otherwise the opening is made in such manner that the punctures lying the farthest from one another are united by a straight incision, accomplished by a number of successive strokes of the knife. Simon urges that the careful and early removal of the echinococcus cysts is of special value toward securing a favorable result. Antiseptic after-treatment, which is not favored by Simon, might, nevertheless, be preferable to the open treatment of the wound.

In view of the entire hopelessness of echinococcus multilocularis, an operation might here also be ventured on, as has been tried by Griesinger and Juergensen, seeing that a cure might possibly be attained.

Other Parasites of the Liver.

Cysticercus Cellulosæ

is very rare in the liver. Thus far we know of no disturbances which might be called forth by the presence of this parasite.

Pentastomum Denticulatum

is the youthful specimen of the pentastomum tænioides which haunts the nasal cavity of the dog. This parasite had formerly been found in various animals, such as goats, squirrels, guinea-pigs, etc. Then Bilharz[1] found it in two dead bodies in Egypt,

[1] Zeitschrift f. wissenschaftl. Zoologie. 4, p. 53. 1852.

although it was falsely considered as identical with the much larger pentastomum constrictum likewise found in Egypt by Bruner. Zenker[1] was the first to discover it in Germany in man. He described it somewhat minutely, and showed that it was by no means a rare guest. It is to be found in other portions of the body besides the liver, especially in the lungs and in the walls of the intestines.

The pentastomum denticulatum is generally to be found on the surface of the liver as a roundish nodule of the size of a pin's head, white in color, generally elevated a little above its surroundings. On more careful inspection it is found that the nodule consists of a very tough, whitish, connective-tissue capsule, which encloses a yellow body, generally calcified, bent in the form of a crescent. It is very difficult to enucleate this kernel without breaking it. If the salts of lime are dissolved in acids, we find the four large claw-shaped feet with their supporting apparatus, as well as, generally, fragments of the skin, which is as clear as glass. The skin is studded with regular rows of fine thorns alternating with rows of double-contoured stigmata.

The statistics of entozoa which Mueller[2] collated from Professor Zenker's post-mortem reports reveal a number of interesting facts with regard to the frequency of the occurrence of pentastomum. The basis upon which they rest are 1,939 autopsies made between the years 1852 and 1862 in Dresden, and 1,755 in Erlangen. The first striking fact to be noticed is that pentastomum did not occur in one of the 631 individuals who were under twenty years of age. Pentastomum was found in 4.69 per cent. of all bodies examined at Dresden, or in 5.16 per cent. of the bodies of all those over twenty years of age; at Erlangen, on the other hand, it occurred in only 1.42 per cent. of all bodies examined, and in 1.9 per cent. of all over twenty years of age. In Dresden the male sex was affected in 5.76 per cent. (6.2 per cent.) of the cases, the females in 3.03 per cent. (3.3 per cent.); in Erlangen the males constituted 1.66 per cent. (2.2 per cent.), the females 1.04 per cent. (1.4 per cent.).

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[1] Zeitschrift f. rationelle Medicin. N. F. V., p. 212. 1854.

[2] Statistik der menschlichen Entozoen. Dissert. Inaug. Erlangen, 1874.

Among 670 bodies of persons over fifteen years old, examined in Kiel during the years of 1873 to 1876, pentastomum denticulatum was found in 1.6 per cent., thus giving similar results to those of Erlangen.

Although thus far no manifestations of disease have been observed in man which it has been possible to refer to the presence of the pentastomum denticulatum, still we must not lose sight of the fact that, according to Leuckart's[1] investigations, the movements of these parasites within the parenchyma of the liver are followed by the gravest disturbances whenever a larger number of the young parasites invade the organ at one time.

The pentastomum belongs to the order of mites. The history of their development has been clearly set forth by Leuckart. The adult animal, the pentastomum tænioides, lives in the nasal cavity of the dog, and in the cavities contiguous to the nose. The male is about fifteen millimetres in length, and the female about eighty-three. The eggs, even before they are laid, show fully developed embryos; they escape mingled with the nasal mucus. If they happen to be taken into the alimentary canal of a suitable animal their envelopes are dissolved, the embryos, with their two pairs of claws, bore through the walls of the alimentary canal, and, by routes that are not fully determined, reach the most varied organs of the body, especially the liver and lungs. Once encapsulated there, they undergo several changes of their envelopes and develop into the pentastomum denticulatum. If, by any means, the encapsulated pentastomum denticulatum now becomes an inmate of the nasal cavity of the dog or wolf, it there develops to sexual maturity.

Psorosperms

have thus far only been found twice in the liver of man. They are egg-shaped bodies, 0.03 to 0.04 mm. long, and 0.012 to 0.02 mm. broad, with a uniform, double-outlined shell, and granular contents. The latter either fills the entire cavity or is merely rolled up in a roundish little heap, while the rest of the space appears clear.

According to Eimer,[2] these psorosperms are gregarinæ at rest; the segmentation of the latter results in the production of psorosperms. The gregarina, either free or enclosed in an epithelial cell, grows into a naked psorosperm, then becomes encapsulated,

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[1] Bau und Entwicklungsgeschichte der Pentastomen. Leipzig, 1860.

[2] Ibid.

and develops the structures similar to the ova of round worms. In these it divides by segmentation into spheres, from which young gregarinæ are developed.

Such psorosperms at times cause a dying off of young rabbits as if by a plague; in such animals the biliary passages in the congested liver appear as sausage-like, distended yellow pouches. On being cut across, a fluid resembling pus escapes from them, which, besides pus-corpuscles and epithelial cells, contains enormous quantities of the structures in question. The same structures are found in the intestine, partly free, partly enclosed in cylindrical epithelium.

Pestilences have also been observed in fowls, called forth by such psorosperms.

Only two cases of psorosperms in the liver have thus far been certainly observed. The first is reported by Gubler.[1] In the liver of a man, forty-five years of age, about twenty globular tumors were found, the tough mucous contents of which revealed well-developed psorosperms, besides larger granular cells, cylindrical epithelium, and cells like pus-corpuscles. One pole of the psorosperms was pointed like that of a microphyle, corresponding in this respect to other descriptions of the same. The second case is reported by Leuckart,[2] according to an epistolary communication of the observer. Dressler (of Prague) found three nodes, varying in size from that of a millet-seed to that of a pea, near to the sharp edge of a human liver; the milk-white broth contained in which revealed, under the microscope, the presence of perfectly developed psorosperms.

The interesting case of Virchow[3] is everywhere still cited as a third instance in point, although Klebs,[4] it is true, mentions it with great doubt. I have, however, shown that in that instance we undoubtedly have to deal with the eggs of the ascaris lumbricoides, which probably originated from a worm that had strayed into the biliary passages.[5]

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[1] Mém. de la Soc. de biologie. 1859. T. V., p. 61.

[2] Parasiten. II., p. 741, with illustration.

[3] Archiv. 18, p. 524. Plate X. Fig. 5.

[4] Patholog. Anatomie. I., p. 528.

[5] This Cyclopædia. Vol. VII., p. 745.

THE DISEASES

OF THE

BILIARY PASSAGES AND PORTAL VEIN.

VON SCHUEPPEL.

DISEASES OF THE BILIARY PASSAGES.

THE close spatial as well as physiological relations which exist between the liver and the biliary apparatus in the narrower sense, *i.e.*, the gall-ducts and their appendage, the gall-bladder, explain the fact that the diseases of the biliary passages have always been described in the closest connection with those of the liver. The observations which may be made concerning the history of diseases of the liver may, therefore, be applied in the main to affections of the biliary passages, or at least to the more common ones. This is also true with reference to the literature of these affections. A connected and independent investigation of the various diseases of the biliary passages has been scarcely attempted hitherto. Some of them, as for instance, those affections which are caused by gall-stones, have, indeed, been exhaustively discussed in monographs; many, however, have been very imperfectly investigated, especially from a clinical standpoint, and our knowledge of them is confined in great part to their anatomo-pathological conditions. But it is especially in this latter relation that, in the course of time, a very large amount of material has been gathered, which is composed, in great part, of a mere collection of cases that have not been critically separated from one another. On the whole, many obscure chapters and very decided gaps may still be detected in the pathology of the biliary passages. Insufficient knowledge of the minute structure and anatomical relations especially of the finest biliary passages can no longer be adduced in explanation of this fact, as might have been done before the discovery of the so-called capillary bile-ducts. Many points still remain to be explained with reference to physiology, both concerning the

chemical constitution of the bile, and especially with regard to the general vital relations of the biliary passages. Only a few features of the symptomatology and diagnosis of certain diseases of these organs have been hitherto recognized, while a well-rounded clinical history has not as yet been formed. The following chapters will contain sufficient proofs of the correctness of these statements. The imperfect character of our knowledge of diseases of the biliary passages finds its expression in the fact that they cannot be discussed from a strictly anatomical, etiological, or symptomatological standpoint, but that, on the other hand, sometimes this, sometimes that principle must be placed in the foreground, and must be accepted as the point of departure in classifying and arranging the diseases under consideration.

Anatomo-Physiological Remarks Concerning the Biliary Passages.

The chief ramifications of the excretory bile-ducts, within the liver, form a branching system of tubes which, either singly or in pairs, accompany the branches of the portal vein and hepatic artery, and are enclosed, like them, in a common connective-tissue sheath (prolongation of Glisson's capsule). The finest terminations of this collection of tubes are each situated between two hepatic lobules, and are, therefore, known as interlobular ducts. They present a diameter of about 25–35 μ ($\mu = 0.001$ mm.). A number of these interlobular ducts approach each acinus of the liver from various sides. Some observers maintain that those interlobular biliary ducts which belong to a single acinus anastomose with one other, so that each acinus is surrounded by a network of the smallest biliary passages. Others deny this and believe that the interlobular biliary ducts terminate in blind extremities. The so-called capillary bile-ducts, or lobular biliary passages, which are situated in the parenchyma of the lobules between the liver-cells and form a close and fine network, are very narrow tubes; their lumen measures from 1.5 to 2 μ. Of those biliary capillaries which are formed entirely by the walls of the secreting glandular cells, and which do not appear to possess a wall, there are as many observed at the surface of each hepatic

lobule, as the latter presents radiating rows of liver-cells, since each row of cells also contains a capillary bile-duct. The latter enters directly into the interlobular duct. At its point of entrance, the small cylindrical epithelium of the latter becomes converted, almost without any transition, into the large secreting hepatic cells, which may be regarded, in a certain sense, as the epithelium of the capillary bile-ducts.

The interlobular biliary passages gradually form larger ducts, which are uniformly directed toward the transverse fissure of the liver. They make their appearance in the fissure as a right and left principal trunk, each of which is about 5 mm. in diameter. In addition, there are three or four smaller branches which are visible in the longitudinal fissure of the liver and empty into the principal ducts. The union of the right and left principal biliary ducts gives rise, in front of the transverse fissure of the liver, to the duct proper of the hepatic cells, or the ductus hepaticus, a canal which presents, on the average, a length of 3 ctm. and a thickness of 6–7 mm.

In addition to the previously described principal ramifications of the biliary passages, there is also a subordinate ramification which is characterized by a tendency to the formation of anastomoses, and constitutes essentially a close network of fine tubes, which is introduced between the biliary ducts belonging to the principal ramifications. Before its entrance into the substance of the liver, the ductus hepaticus and its principal trunks give off superficial fine branches, which ramify in the connective tissue of the fissures of the liver, and anastomose freely with one another. These networks of ducts, situated outside of the liver, are connected with others of a similar nature which are situated in Glisson's capsule, in the vicinity of the larger branches of the portal vein and the biliary ducts, and receive their branches from the latter. All of these meshes send fine twigs into the parenchyma of the liver, which finally also terminate in interlobular biliary ducts. This subordinate ramification of the biliary excretory ducts, especially of that part which is situated in front of the transverse fissure,[1] merits attention with reference

[1] Represented in *Henle*, Handb. d. system. Anat. II. (Visceral Anatomy) 1866, p. 202.

to pathology, because it serves perhaps to explain certain phenomena connected with the discharge of bile, which would otherwise be inexplicable. When, for instance, the chief right branch of the ductus hepaticus is impervious at a short distance from its entrance into the latter, the possibility of the discharge of bile from the right lobe of the liver is not excluded absolutely, as the bile would pass from the chief right branch, by means of the subordinate ramification, into the pervious left chief branch, and could, therefore, make its escape in a normal manner.

The ductus hepaticus joins, at an acute angle, the somewhat narrower excretory duct of the gall-bladder, the ductus cysticus, to form the common excretory duct, or ductus choledochus. I have found that the average length of the ductus cysticus is 4.8 ctm. At its entrance into the neck of the gall-bladder it is very strongly curved, and indeed almost bent on itself. Its diameter, as a rule, is only two-thirds of that of the hepatic duct. The lumen of the cystic duct presents a different appearance from that of the other biliary ducts. When distended it does not appear smooth, but presents rounded recesses, between which are deep, contracted portions, so that it looks like the large intestine on a small scale. The narrowed parts correspond to crescentic projections upon the inner surface of the wall. These projections, which are described as folds in the mucous membrane of the duct, and are known as Heister's valves, only occupy about one-half of the circumference of the canal, and are situated alternately, at intervals which are not quite equal to one another, so that the axis of the canal describes a rather sharply curved wavy line. It is evident that this condition of the canal is not without an adverse influence upon the movement of its contents, at least in the case of solid bodies, such as gall-stones.

The gall-bladder, which is adherent to the lower surface of the liver in the right longitudinal fissure, and is of an elongated, pyriform shape, contains about 50 c.c. of fluid when moderately filled. The fundus of the gall-bladder, which is situated on a plane with the anterior border of the liver, is directed toward the cartilage of the eighth rib, at the point where the right parasternal line meets the ribs.

The ductus choledochus is, on the average, 7 ctm. long in the

adult, and presents nearly the same diameter as the hepatic duct, or is somewhat narrower than the latter. It is enclosed in a fold of the peritoneum known as the hepatico-duodenal ligament, and first runs downward, past the posterior wall of the duodenum, and then curves gently to the concave (median) side of the vertical portion of the latter. The hepatic artery and portal vein are also situated in the above-mentioned peritoneal fold, in close apposition to and parallel with the common biliary duct, with which they are connected by loose cellular tissue; the hepatic artery is situated to the left of the common gall-duct, and the portal vein behind the other two. Before the ductus choledochus enters the wall of the duodenum it approaches very closely the pancreas and its principal excretory duct. After it has reached the concavity of the duodenum it sometimes passes in a more or less shallow groove on the posterior surface of the head of the pancreas, but at other times it perforates the head of this organ, so that it is surrounded by glandular tissue on all sides. Sometimes only a few lobules of the gland project beyond its posterior wall, at others it is enclosed on all sides by a thick layer of glandular tissue. According to the observations of O. Wyss, the common gall-duct passed alongside of the head of the pancreas in fifteen cases out of twenty-two. Wyss[1] has with justice attached great importance to these relations of the gall-duct to the head of the pancreas. In fact, in those cases in which the ductus choledochus passes by the side of the pancreas, the former will only become displaced when the head of the pancreas undergoes enlargement. In such a case only a very considerable enlargement of the pancreas, which, at the same time, produces traction, flexion, or dislocation of the parts, would produce compression of the gall-duct. But if the latter passes through the substance of the pancreas a much less marked hypertrophy of the head of this organ will be sufficient to produce closure of its lumen, and, therefore, stasis of the bile and icterus.

The wall of the duodenum is penetrated obliquely by the terminal portion of the ductus choledochus; the canal first passes through the muscular coat of the intestine, and then for a certain

[1] Zur Ætiologie des Stanungs-Icterus. Virch. Arch., 36, p. 454.

distance beneath the mucous membrane, before it empties into the cavity of the intestine, in a slightly conical projection of its mucous membrane, viz., the caruncula duodenalis major. This so-called *pars intestinalis*[1] of the ductus choledochus is 2.4 ctm. in length. It is normally considerably smaller than the other part of the canal, as I have found that the terminal portion, when cut open and spread out, is only 0.5 ctm. wide, *i.e.*, its diameter would not even amount to 2 mm. After the ductus choledochus has passed between the muscular and mucous coats of the duodenum, it receives, at an acute angle, the principal excretory duct of the pancreas, which has passed through the circular muscular coat of the intestine at the same place and in the same direction. That portion which is common to both canals, and which is 8–10 mm. in length, bears the not very apt title of diverticulum Vateri. The direction of the *pars intestinalis choledochi* forms a very acute angle with the longitudinal axis of the intestinal tract. The narrowness of the pars intestinalis and its opening enables us to comprehend that vigorous pressure upon the contents of the biliary passages will serve to force them out in a jet, as has been stated by various observers. It is also evident that a moderate amount of swelling of the mucous membrane will be sufficient to entirely occlude the lumen of the terminal portion of the common gall-duct.

The walls of the ductus choledochus, cysticus, and hepaticus, which are 0.6 mm. in thickness, and those of the larger branches of the latter, present two rather closely connected layers, of which the inner may be termed the mucous membrane and the outer the fibrous coat. The mucous membrane contains a very close network of capillaries, is rich in very fine elastic fibres, and is covered with a single layer of elongated cylindrical epithelium. The fibrous layer, on the other hand, contains very few blood-vessels. Some remarks will be subsequently made concerning the muscular elements which it contains. The medium-sized biliary canals in the liver present walls with only a single layer; their epithelium is not as elongated as that of the larger canals.

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[1] *Luschka*, Die Pars intestinalis des gemeinsamen Gallenganges. Prager Vierteljahrschr. Bd. 103, p. 86 et seq. (With instructive plates.)

In the smallest canals the walls are reduced to an almost structureless basement membrane, which is covered with small cylindrical epithelium. The lumen of the interlobular canals is only 5–7 μ in width, or about one-fifth of the average diameter of the canal.

The larger bile-ducts, down to those of 0.25 mm. diameter, are provided with numerous small glands which are lodged in the walls of the canals and consist of round or elongated glandular vesicles, which are often shaped like the vermiform appendix. Their openings appear like small punctate pores upon the inner surface of the canal. These so-called bile-duct glands possess no specific epithelium; they present the cylindrical epithelium, which is similar to that of the canals into which they empty, and various views have been entertained with regard to their significance. They should properly be regarded as involutions of the lumen of the canals (Henle) and not of the entire wall. We can only entertain surmises with regard to their functions, but they probably possess no specific property whatever. Their epithelium, like that of the biliary ducts themselves, is probably engaged in the production of mucus.

The mucous membrane of the gall-bladder, which is distinguished by numerous projections which are united into a network upon their free surface, possesses an extremely rich capillary meshwork and a single layer of cylindrical epithelium. A layer which is situated beneath the mucous membrane and is composed of freely anastomosing bands of involuntary muscular fibres, has been described by some anatomists as a special muscular coat, but is regarded by Henle as a part of the mucous membrane. The muscular coat is surrounded by a connective-tissue layer, and this, upon the free surface of the gall-bladder, by the peritoneum. The mucous membrane of the gall-bladder is very poorly supplied with glands. Luschka found from five to sixteen in the submucous tissue; they must be regarded as mucus-producing structures.

The question of the presence of muscular elements in the walls of the biliary ducts is important from a pathological standpoint and has been freely discussed. The movement of the bile, and especially the changes in the position of solid bodies (gall-

stones) within the biliary passages require forces which were naturally attributed to contractile elements in the walls of these canals. But we know only with regard to the gall-bladder that this organ possesses a layer of anastomosing bundles of smooth muscular fibres beneath the mucous membrane. The presence of muscular fibres in the biliary passages, however, and even in the largest ones, has not been satisfactorily demonstrated even at the present time. The examination of the excretory bile-ducts with regard to their contractility under the stimulus of electricity in the body of a decapitated individual gave negative results in the hands of one observer (Henle), while others have obtained positive results from this experiment (Dietrich, Gerlach, Herz). The majority of histologists only admit the presence of scattered involuntary muscular fibres in the fibrous layer of the larger bile-ducts, and all are united in the opinion that there is no connected muscular layer in the excretory bile-ducts. Heidenhain alone, who made his histological investigations in this regard upon animals (rabbits), thinks that he has shown evidence of the presence of numerous contractile elements in the excretory ducts of the liver. He employed the chloride of palladium, which was recommended by F. E. Schulze as a reagent for smooth muscular fibres, and believes that he has undeniably shown, with its aid, the presence of circular as well as longitudinal bundles of contractile cells in the connective-tissue layer of the larger and medium-sized biliary canals. The layer containing the muscular fibres presented not a few non-medullated nerve-fibres. Certain physiological phenomena[1] also testify, according to Heidenhain, to the presence of contractile elements in the walls of the biliary canals.

The study of diseases of the biliary passages has hitherto received very little aid from physiology. From a physiological standpoint we are, for the present, less interested with the bile itself, with its chemical constitution, and its relations to digestion; we are, on the contrary, much more interested in everything which pertains to the movement of the bile within the

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[1] *Heidenhain*, Studien aus dem physiolog. Instit. in Breslau. IV. Heft. 1868, p. 242 et seq.

canals. *A priori*, we should expect that the constitution of the bile would, under certain circumstances, not be without influence upon the condition of the walls of the canals with which they are continually in contact, and, on the contrary, it may be presumed that the normal or abnormal condition of the biliary passages would exert a reciprocal action upon the formation of the bile. The latter view would follow necessarily, if Robin's opinion were substantiated, that the bile is not the product of the glycogen-forming liver, but of the glands of the biliary canals. But the problems involved in these questions have been barely formulated, much less answered. The opinion held by Budd, however, merits attention; he believed that the bile, under certain circumstances, especially when it had become somewhat concentrated from its continued presence in the gall-bladder, acquired a certain degree of acridness, and might, therefore, act upon the walls of the biliary canals as a source of inflammation. Not even a surmise has been made, however, as to the character of this acridness, apart from the greater amount of concentration of the bile.

With regard to the movement of the bile, we must first determine the propelling forces by which the flow of this secretion from the bile-ducts is effected. Attention has been already drawn to the uncertainty with regard to the presence or absence of muscular elements in the walls of the bile-ducts. It appears, indeed, as if the muscular fibres, which may be present, could possess very little significance with regard to the movement of the fluid. Under ordinary circumstances the pressure in the capillaries, *i.e.*, the pressure due to the secretion, is regarded as the chief motor force. Respiration also acts as an auxiliary. At each inspiration pressure is produced upon the liver and the entire biliary apparatus, and thus aids the flow of bile. In addition, the pressure of the adjacent organs, of the intestines, the abdominal walls, etc., must also be mentioned as one of the auxiliaries to the flow of bile. Contractions of the gall-bladder are only important with reference to the contents of the latter, and to the bile in the ductus cysticus and ductus choledochus, when its escape into the intestines does not meet with any obstacle. But if the latter condition is present, if the mouth of the ductus

choledochus, for example, is closed by a plug of mucus, by swelling of the mucous membrane, etc., the contractions of the gall-bladder will cause an increase of pressure in the various biliary passages, and also in those situated within the liver, which may increase to such an extent that it finally overcomes the obstruction in the ductus choledochus.

The bile may either flow directly from the hepatic canals into the duodenum, or passes from the ductus hepaticus and ductus choledochus through the ductus cysticus into the gall-bladder, and accumulates in the latter, until, at a later period, it is poured in large quantity upon the substances which are undergoing digestion in the intestines. The accumulation of bile in the gall-bladder occurs in the interval between two periods of digestion; a small portion escapes into the intestines in the fasting condition. The cause of the accumulation of bile in the gall-bladder consists in the fact that its secretion continues while the orifice of the ductus choledochus is narrowed by the muscular fibres in the intestinal walls, which are contracted during the fasting condition. This is also shown by experimentation. If air is blown from the hepatic duct into the excretory canals, the gall-bladder will be filled before the air passes into the intestines; there is, therefore, a relative obstruction at the intestinal end of the ductus choledochus. We may convince ourselves, however, by vivisection, that the bile flows in drops into the intestines, even in the fasting condition. In the gall-bladder, the bile becomes thicker, more viscid (richer in mucus), more alkaline, and of a darker color.

In prolonged fasting the gall-bladder is always filled. Its contractions occur through reflex means, as soon as the mucous membrane in the neighborhood of the orifice of the ductus choledochus becomes irritated, an event which happens from its mere contact with the digestive substances which have passed into the duodenum. If the duodenum is opened in a living animal and the caruncula duodenalis major is irritated by dropping vinegar upon it, etc., a profuse discharge of bile into the intestines occurs at once and continues for several minutes. The respiratory movements, and the pressure of the full duodenum and intestines upon the gall-bladder, are of secondary importance. The effect of the latter is shown by the fact that in dogs, in whom a biliary fistula

has been produced, the bile is discharged more copiously during defecation and the act of vomiting.

We may here refer to the fact[1] that the site of the absorption of bile (in icterus) is not identical with that of its secretion, and the formation of bile occurs while its absorption continues. Absorption occurs through the walls of the biliary passages and their blood-vessels and lymphatics; secretion, however, is effected by the hepatic cells.

The amount of bile secreted in a given time is only important in those cases in which its escape into the intestines is prevented. But even then its importance is not very great, as the quantity is subjected to great variations from inspissation or absorption.

Catarrhal Inflammation of the Biliary Canals.

(*Icterus catarrhalis, gastro-duodenalis, etc.—Cholangoitis catarrhalis.*)

Friedr. Hoffman, Medicinæ rational. systema. Tom. IV. Pars IV., p. 351. Halæ, 1737 (De cachexia icterica).—*Morgagni*, De sedibus et causis morborum. Epistola XXXVI. (De ictero et calculis biliosis.)—*Bamberger*, Krankheiten des Gallengefässapparates, in Virch. Handb. d. spec. Pathol. u. Therap., VI. Bd. 1 Abth. S. 614. Erlangen, 1855.—*Henoch*, Klinik d. Unterleibskrankh. I. Bd. 2 Aufl. Berlin, 1855.—*Frerichs*, Klinik d. Leberkrankh. II. Bd. S. 416. Braunschweig, 1861.—*Virchow*, Ueber das Vorkommen u. den Nachweis des hepatogenen, insbesondere des katarrhalische Icterus. Archiv f. Path. Anat. XXXII., 1865, S. 117.—*O. Wyss*, Zur Lehre vom katarrhalischen Icterus. Arch. d. Heilkunde. VIII., 1867, S. 469.—*Jaccoud*, Leçons de clinique médicale. Paris, 1867, p. 279.—*Ebstein*, Katarrh d. makroskopisch sichtbaren feinsten Gallengänge, etc. Arch. d. Heilk. 1867. S. 506 u. IX. 1868. S. 219.—*Gerhardt*, Ueber Icterus gastro-duodenalis. Volkmann's Sammlung klinischer Vorträge. No. 17. 1871.—*Stitzer*, Ueber Icterus epidemicus. Wien. med. Presse. 1876. No. 12–17.—*Klingelhaeffer*, Beitrag zum Icterus epidemicus. Berl. klin. Wochensch. 1876. No. 6, u. 1877. No. 48.—*Koehnhorn*, Ueber Gelbsucht-Epidemien. Berl. klin. Wochenschr. 1877. No. 7.—*Kruell*, Zur Behandlung des Icterus catarrhalis. Berl. klin. Wochenschr. 1877. No. 12, S. 159.—*Froehlich*, Ueber Icterus-Epidemien. Deutsch. Arch. f. klin. Med. 24 Bd. S. 394. 1879.

Catarrhal inflammation occurs with almost as great frequency in the biliary canals as in other mucous membranes. But it is

[1] Cf. *Heidenhain*, l. c.

not, by any means, characterized by such prominent symptoms that its existence is thereby demonstrated in all cases. Jaundice is the most important and often the only symptom of catarrh of the biliary canals. But this can only develop when the inflammatory swelling of the mucous membrane of the biliary passages is great enough, and the secretion furnished by the mucous membrane is copious and viscid enough, to produce closure of the biliary ducts and therefore interfere, at least in part, with the escape of bile. When obstruction and absorption of the bile does not occur, the other symptoms which may be present will not suffice to permit a diagnosis of catarrh of the bile-ducts with any degree of certainty. It is for this reason that it has become customary to employ the term "icterus catarrhalis" as almost synonymous with "catarrh of the bile-ducts," although the ideas conveyed by these two terms do not by any means cover one another, as there are many cases of catarrh of the bile-ducts which are not associated with jaundice. Those cases of catarrhal icterus, which, apart from the jaundice and the phenomena immediately dependent upon it, present no other symptoms, have been termed icterus simplex, formerly also icterus essentialis.

The prominent symptom of catarrh of the bile-ducts, viz., jaundice, is not alone dependent upon the degree of swelling of the mucous membrane, or the constitution and quantity of the catarrhal secretion, but is also affected, and perhaps to a still greater extent, by the situation and extent of the catarrhal process in the distribution of these organs. Thus, for instance, catarrh of the ductus cysticus cannot produce jaundice, even when it gives rise to complete closure of its lumen by the swollen mucous membrane. It is very apparent, however, *a priori*, that closure of the pars intestinalis of the ductus choledochus will most readily lead to obstruction of the bile and to jaundice. It has even been held that in catarrhal icterus only the pars intestinalis of the ductus choledochus is involved, and that catarrhal icterus only means catarrh of the pars intestinalis of the ductus choledochus (Virchow, l. s. c.). This statement is very plausible, and has obtained many adherents; nevertheless it is incorrect. Wyss has shown by experimental means that the catarrhal closure of the finer bile-ducts within the liver may also lead to an

obstruction-jaundice, which, however, can be distinguished from the ordinary gastro-duodenal icterus by a somewhat different symptomatology. Wyss and Ebstein have shown, with regard to the jaundice which accompanies acute phosphorus-poisoning, that it is due to a catarrh of the finer bile-ducts which are still visible to the naked eye. Within the last few years, moreover, the boundaries of so-called hematogenic icterus have become more and more circumscribed, and it has been rendered probable that many cases of jaundice, which are not due to coarse mechanical lesions, belong to the category of obstructive-jaundice, the causes of which must be sought for in a catarrh of the pars intestinalis of the ductus choledochus or of the hepatic bile-ducts. This is true of icterus neonatorum, and of the jaundice occurring in the course of typhoid fever, pyæmia, pneumonia, and other, especially dyscrasic, diseases (syphilis, lead colic). It becomes difficult, under such circumstances, to satisfactorily define the boundaries of catarrhal icterus, which is more extensive than has been hitherto supposed. A limitation will, however, be found in the accompanying remarks, since we do not treat of jaundice as such, but rather of the causal anatomical changes, *i.e.*, of the catarrh of the bile-ducts; we will refer, however, especially to those cases in which the catarrh is an independent disorder or at least constitutes the chief disturbance.

Etiology.

Catarrh of the bile-ducts occurs with relative infrequency from causes which act directly upon the mucous membrane of the biliary passages. In the majority of cases the disease is due to a catarrhal affection of the duodenal mucous membrane, which is almost always combined with catarrh (usually acute or subacute) of the stomach and intestines, spreads to the pars intestinalis of the common bile-duct, and is propagated thence to the capillary hepatic bile-ducts and to the gall-bladder. Among forty-one cases of this disease, Frerichs[1] observed this manner of development no less than thirty-one times (more than eighty per

[1] Klinik d. Leberkrankh. II. S. 418.

cent.). All those factors, therefore, which may give rise to gastro-duodenal catarrh, must be enumerated among the exciting causes of catarrh of the bile-ducts. They include, in most cases, indigestion, which has been produced by the ingestion of articles of food, which, on account of their quantity or quality, have caused an abnormal condition of irritation of the gastric and intestinal mucous membrane. A too copious meal, the ingestion of very fat food which is digested with difficulty, spoiled food, which gives rise to abnormal processes of decomposition within the stomach, too hot or too cold drinks (ice), and especially excessive drinking, must be very frequently regarded as causes of gastro-intestinal catarrh, to which catarrhal jaundice is due. Very acrid substances, also, which irritate the gastric mucous membrane, such as strong spirituous liquors, and many medicinal articles, especially emetics and cathartics, belong to the same category as the above-mentioned factors.

Next in importance to "spoiled stomach" as causes of catarrhal jaundice come colds and exposure, together with various influences connected with the atmosphere, but which cannot be more closely defined (often, probably, of a miasmatic character). In many cases factors of this kind may act by giving rise to gastro-duodenal catarrh, which is then propagated to the bile-ducts. But there is no doubt that this does not occur in all cases. Many patients know of no other factor beyond exposure as the cause of the catarrhal icterus from which they suffer, and nevertheless the symptoms of gastric and intestinal catarrh are entirely absent. The connection between exposure and catarrh of the bile-ducts remains as obscure as in the majority of diseases arising from "colds." Inasmuch as colds develop most readily at times in which there is a rapid and frequent change of temperature, this is explanatory of the fact that cases of catarrhal icterus which have developed in this manner are most frequent in spring and autumn. This so-called icterus vernalis, autumnalis, etc., does not present any peculiarity.

From time to time veritable epidemics[1] and endemics of

[1] Such epidemics have been described in ancient as well as modern and even the most recent times (*Decaisne* and *Sée* in Paris: Gaz. des hôpitaux, 1872, No. 26; *Rizet*, *Rehn*, *Diamantopulos*, Athens; *Stitzer*, *Koehnhorn*, *Klingelhoeffer*, and others). Thus,

catarrhal jaundice are observed, usually in its mildest form. In such cases we are at once inclined to think of atmospheric influences. The suspicion is forced upon us, with regard to certain epidemics, that miasmatic influences have at least aided in their production as, for instance, in the one described by Rizet,[1] in which the cleansing of a ditch in a fortress of Anas was the exciting cause for the outbreak of the endemic in which, at first, only the laborers engaged in this work were affected with jaundice. As a rule, individuals of every age and condition are indiscriminately affected in epidemic icterus. Exceptionally certain classes of the population suffer more or less exclusively. In the epidemic described by Rehn in Hanau, children were almost alone affected. Stitzer[2] describes two "house-epidemics," in one of which five, in the other fourteen persons were affected, and considers the cause of the infection to have been bacteria, developing from decomposing substances which had escaped from a defective drain-pipe in the kitchen. Koehnhorn,[3] Lindemann,[4] Sée, and others, describe military epidemics, which occurred among certain classes of soldiers, living in garrison during times of peace as well as on the field. I know of a small epidemic of this kind in the Tuebingen garrison, in which the recruits alone suffered. Koehnhorn endeavors to show that the cause of the military epidemic observed by him consisted in insufficient variety in the diet of the soldiers. Froehlich[5] has very recently compiled the statistics of more than thirty hitherto reported epidemics of icterus, and in connection therewith has described four military epidemics observed by himself, in which the recruits were alone affected. Froehlich distinguishes two varieties of icterus epidemics. One form, which occurs in Europe, and especially in Germany, presents itself symptom-

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Decaisne, for example, reports an epidemic of "essential icterus" which prevailed in Paris and its vicinity in the autumn of 1871. Cf. Compt. rendus de l'acad. des sciences. 1871, p. 1486.

[1] Cf. *Virchow* u. *Hirsch*, Jahresber., etc., f. 1867. II. S. 157.

[2] Wien. Med. Presse. 1876. No. 12–17.

[3] Berl. klin. Wochenschr. 1877. No. 7.

[4] Deutsche Zeitschr. f. pract. Med. Redig. *v. Kunze.* 1874. No. 45.

[5] Deutsch. Arch. f. klin. Med. Bd. 24, S. 394. 1879.

atically as ordinary catarrhal jaundice, and is in no respect distinguishable from sporadic cases of the disease, not even with reference to etiology. The other form, which is generally observed in hot climates, though sometimes also in France, appears, however, to be closely related to yellow fever, and in fact to be only a modification of the latter. It is especially this variety which presents cases of acute yellow atrophy of the liver, although they are not entirely absent in the first form.

Among those noxious influences which act directly upon the mucous membrane of the bile-ducts and produce catarrh, the circulatory disturbances of the liver merit the chief attention in point of frequency; this is especially true of venous stasis of the blood in this organ, in which the walls of those bile-ducts which are situated within the liver are also implicated. Stases of blood in all organs, and certainly also in the bile-ducts, are a frequent cause of catarrh. The stases of blood in the liver which accompany emphysema of the lungs, mitral regurgitation, degeneration and insufficiency of the muscular tissue of the heart, etc., may therefore, in addition to other factors, be taken into consideration in the explanation of icterus occurring in these diseases.

Certain poisons, especially acute phosphorus-poisoning, and certain infectious conditions, such as cholera, typhus, etc., are notoriously attended with catarrh of the bile-ducts, if not always with icterus. We may suppose that, in these cases, a poison which is present in the blood acts directly upon the mucous membrane of the bile-duct and gives rise to inflammation. In many cases of this kind, however, the existence of gastro-duodenal catarrh, which has spread to the bile-ducts, must also be taken into consideration. We also know that intermittent fever, syphilis, and other dyscrasiæ, may act as causal factors in catarrh of the bile-ducts. We can only entertain surmises with regard to the closer connection between the symptoms in all of these cases.

Direct irritation of the mucous membrane of the biliary passages is effected most evidently (because done in a coarse mechanical manner) by bodies which partake, more or less, of a foreign character, and are in prolonged contact with the mucous mem-

brane. These most frequently include gall-stones, more rarely living parasites (round worms, distomata) which, on account of their presence in the gall-bladder and larger bile-ducts, give rise to inflammation of a primarily catarrhal character, sometimes localized, sometimes diffused over all the canals. Cases of this kind are distinguished by the severe character of the anatomical lesions, the tendency to ulceration, and even perforation of the bile-ducts.

These will be fully discussed, at a later period, in special chapters. On the other hand, we must not omit mention of the fact that the bile itself may, under certain circumstances, act as a source of inflammation upon the mucous membrane of the canals. In particular, the bile which has for a long time remained in the gall-bladder, and has thereby become inspissated, as, for instance, in prolonged fasting, is regarded as a cause of catarrh of the mucous membrane of the organ. Well-defined chemical changes, abnormal transformations or additions of foreign substances (so-called acridities) have, however, not been hitherto demonstrated as the cause for the inflammation-producing quality of the bile. Perhaps the catarrh of the bile-ducts, which occurs in dyscrasic affections, may also be attributed to an abnormal constitution of the bile.

The predisposition to catarrhal jaundice is almost equal in both sexes. The disease occurs much more frequently, however, in youth than at a more advanced age.

Pathological Anatomy.

Simple catarrh of the bile-ducts is quite often found accidentally in autopsies upon individuals who have presented none of its symptoms during life. On the other hand, we do not find very frequent opportunity of making an autopsy in those cases in which, to judge from the symptoms observed, we were justified in diagnosing well-marked catarrh of the bile-ducts. In the cadaver, catarrh of the larger bile-ducts is less marked by the hyperæmia and redness which were undoubtedly present during life, and which, if they are at all visible after death, are commonly concealed by imbibition of the biliary coloring-matter by

the mucous membrane of the bile-ducts. We must pay more attention to a certain amount of swelling, flaccidity, and succulence of the mucous membrane, which may even attain the condition of œdema in parts, and to the signs of increased secretion and copious production of cells upon the surface of the mucous membrane. The bile-ducts are found filled with turbid bile mixed with mucus or with a grayish white, very turbid, mucoid substance, which is very rich in desquamated cylindrical epithelium-cells, that have partially undergone myxomatous degeneration. The condition of the pars intestinalis of the common bile-duct is of especial importance, both because the inflammatory affection of the mucous membrane usually spreads backward to the smaller bile-ducts, and especially from the fact that the presence or absence of the most important symptom, viz., jaundice, is chiefly determined by the anatomical condition of the pars intestinalis choledochi. Even a moderate catarrhal swelling of this part will suffice to produce a certain amount, if not absolute, closure of the excretory duct, and therefore stasis of bile and icterus. Care and judgment are requisite in order to determine upon the cadaver whether this part was closed during life. We must remember that a swelling of the mucous membrane, which may have rendered the flow of bile into the intestine impossible during life, may disappear after death, and that a sound may be passed post-mortem through the terminal end of the common bile-duct, and the bile be squeezed out of the latter into the intestines, although the pressure, to which the bile is subject in the excretory ducts, was insufficient to effect this during life. The previous existence of occlusion of the pars intestinalis of the common bile-duct from a swelling of the mucous membrane may be regarded as demonstrated, when its opening presents a certain amount of succulence and swelling of the tissue, perhaps even œdema, hyperæmia, and hemorrhage into the mucous membrane, when a whitish plug of mucus may be pressed out of the extra-intestinal end of the bile-duct, and the mucous membrane in the region of the narrowed pars intestinalis is found to be colorless, although the remaining portion (situated further backward) is dilated and appears to be tinged with bile. The white color (untinged with bile) of the occluding plug of mucus, and the

absence of imbibition of the mucous membrane of the pars intestinalis with bile show that this portion of the canal has, for a certain length of time, not come in contact with the bile, and that it has been impermeable. In cases in which the flow of bile into the intestine is prevented by catarrh of the pars intestinalis choledochi, the bile which has been secreted during this period will accumulate in the gall-bladder and give rise to more or less marked dilatation of the latter. A certain amount of dilatation will also be produced, by the stasis of the bile, in the larger bile-ducts inside as well as outside the liver. The widened fundus of the immoderately distended gall-bladder sometimes projects from 3 to 6 or more ctm. beneath the sharp border of the liver. At the height of the affection the entire liver is slightly enlarged, its tissue presents more or less imbibition of bile, and is of a yellowish brown or brownish green color. The mucous membrane of the stomach and duodenum presents the signs of acute catarrh: redness and swelling, and a thick coating of turbid, not very tough mucus. The simple acute catarrh of the bile-ducts, especially of the pars intestinalis choledochi and the gall-bladder, which has been just described, usually subsides in a few weeks without leaving any traces, the swelling of the mucous membrane of the bile-ducts disappears, the secretion of bile returns to the normal, the flow occurs without interference, and the entire biliary apparatus presents no further abnormal conditions. After the disease has, in the main, run its course, it occurs, in exceptional cases, that a few bile-ducts within the liver remain obstructed by colorless, firm plugs of mucus. In such an event, scattered spots are found in the liver tinged with bile, while the remainder of the gland has regained its normal appearance.

The anatomical appearances in the disease are very different when the terminal portion of the common bile-duct has remained pervious, as occurs, for instance, in acute phosphorus-poisoning, while the finer hepatic ducts, which are still visible to the naked eye, constitute the chief seat of the catarrh. The large excretory ducts and the gall-bladder are then found to be only moderately filled with pale yellow bile or almost entirely empty. Upon making sections through the liver, however, it is

found that the finer bile-ducts, which follow the branches of the portal vein, are completely filled with tough, turbid, almost white plugs of mucoid consistence, which, upon microscopical examination, are found to be almost entirely composed of desquamated cylindrical epithelium-cells of the bile-ducts.

When the catarrh is limited to the gall-bladder and the ductus cysticus, while the choledochus and hepatic ducts are unaffected, the gall-bladder appears to be moderately distended by inspissated, tough, blackish green bile, which is mixed with a large amount of opaque, grayish yellow mucus. Or the bile is entirely wanting and the gall-bladder is filled with opaque, pale mucus or a muco-purulent mass; the mucous membrane, is however, markedly swollen and succulent, in some places strongly congested, in others anæmic, of a bright yellow color and covered with a thick layer of mucus; superficial ulceration may also be occasionally observed. The catarrh of the gall-bladder produced by foreign bodies (gall-stones) presents a similar character, with the exception that more marked tissue-changes, especially ulcerative processes, make their appearance. These will be discussed, however, at a later period.

In the rare cases in which catarrhal jaundice assumes a chronic course it may happen that all the bile-ducts, which are visible to the naked eye, are not only found filled with a thin, muco-purulent, bright yellowish gray (often almost colorless) fluid, but are also considerably dilated. The mucous membrane of the bile-ducts, in such cases, is pale, flaccid, thickened, the hepatic tissue stained with bile, the entire organ swollen, the walls of the gall-bladder œdematous. Such a catarrh of the bile-ducts is, however, very rarely observed, and only when the terminal portion of the ductus choledochus is permanently occluded.

Pathology.

General Clinical History.

The clinical history of catarrh of the bile-ducts presents various differences, according to the mode of development, the situation, and the extent of the inflammation. In ordinary cases

of catarrhal jaundice the disease begins immediately after an attack of indigestion or after a "cold," with the symptoms of gastric catarrh. The patient experiences a sensation of pressure and fulness in the region of the stomach, complains of nausea and frequent eructations; vomiting is sometimes observed. Headache then makes its appearance, with slight chilly sensations, tendency to vertigo, unwillingness to perform bodily or mental work, general torpor and lassitude; the latter symptoms sometimes attain such severity that we may be led to apprehend the development of typhoid fever. Anorexia is present, there is an antipathy to food, especially to very fatty articles; while, on the other hand, the thirst is increased and there is a desire for cold and acid drinks. The tongue presents a white coating and is somewhat swollen. The patient experiences a pasty, bitter, or other abnormal taste in the mouth. Slight febrile disturbance is often present in the beginning of the disease, though fever may be altogether wanting during its entire course. Constipation is usually present, but diarrhœa is quite frequently observed when the intestinal tract is more seriously affected.

After these symptoms have lasted four to five days (often, however, one to two weeks), the signs of jaundice gradually develop. A faint yellowish tinge is visible upon the conjunctiva; this becomes progressively deeper and more intense, and spreads to the remainder of the body in the next few days. At the same time the dry stools lose their color and become pale gray, while the urine is dark, and a chemical examination shows the presence of the coloring matters of the bile and of the biliary acids. Upon the appearance of icterus the rapidity of the pulse, which is originally somewhat increased, sinks below the normal, sometimes even to fifty beats per minute. The patients complain quite frequently of pruritus, which is especially annoying at night. Xanthopsia, on the other hand, is only exceptionally present. The patients usually present a morose, irritable disposition; sleep is generally restless and broken by dreams. Upon physical exploration of the abdomen the epigastrium is found to be somewhat distended, the liver somewhat enlarged and projecting two to three ctm. beyond the arch of the ribs. The right hypochondrium is sensitive on pressure; in addition,

the patient also experiences at times, in the region of the liver, a dull pressure or even a darting pain, which, however, only attains slight intensity. In many cases the dilated gall-bladder appears at the border of the liver, corresponding to the outer edge of the rectus abdominis, as a tumor, which is recognizable on percussion and, under certain circumstances, on palpation, and extends over the circumference of a dollar piece.

In favorable cases, such as are usually met with, the disease has, in the main, run its course after a period of ten to fourteen days. The subjective symptoms, at least, are usually not of any moment after this period. The end of the disease does not appear suddenly with "critical discharges," but occurs very gradually. The return of the appetite is, as a rule, the first sign of beginning recovery; then the other symptoms of gastro-intestinal catarrh disappear. Finally, the jaundice also disappears, the stools become slightly, then more strongly, tinged with bile, while the bile-pigment gradually disappears in the urine. The integument then recovers its normal color, though three to four weeks usually elapse from the beginning of the disease before this occurs.

In rare cases the disease is much more obstinate; three to four months then elapse before the gastro-intestinal catarrh subsides, and the bile again pursues its regular course into the intestines. Under such circumstances striking emaciation and very marked anæmia generally develop, and the patients require a long period before recovery fully occurs.

Symptomatology.

According to the preceding description, the factors which constitute the clinical history of ordinary catarrhal jaundice are the three following: 1, catarrh of the stomach and intestines, upon which the general disturbance and, at times, the fever depend; 2, the jaundice; and 3, the local symptoms on the part of the liver and gall-bladder. The following remarks will hold good with regard to the various relations of these three factors to one another:

We have previously stated with reference to the gastric catarrh,

that it is not by any means present in all cases of this disease. Quite frequently (and especially in so-called epidemic icterus) the general condition is scarcely affected, the tongue is not coated, the appetite undisturbed, the thirst is very moderate; slight constipation is alone observed. When the symptoms of gastric catarrh are present, they precede the development of the jaundice by three to five days. This period is requisite for the spread of the catarrh from the stomach to the duodenum and ductus choledochus, and for the development of stasis of the bile to such an extent that absorption of the latter must occur. The catarrh is more frequently accompanied by constipation than by diarrhœa, a fact which tends to show that the catarrhal process in the intestinal canal does not extend far beyond the duodenum, or does not attain great severity. The fever present in individual cases, and which is almost always very slight, is also due to the gastric catarrh. It is a remarkable fact that the symptoms of gastric catarrh, and especially the disturbances in the general condition, undergo marked improvement very soon after the development of jaundice. Usually, however, the initial symptoms are combined with the jaundice for a number of days. The jaundice generally lasts a few days longer than the gastric catarrh; in much rarer instances the former disappears, while the disturbances of digestion continue.

The jaundice, which accompanies catarrh of the bile-ducts, arises from mechanical causes, and is an obstruction-jaundice of the purest form. It is due to the occlusion of the (larger) bile-ducts by the inflammatory swelling of the mucous membrane and by tough plugs of mucus. The occluded portion corresponds, as a rule, to the pars intestinalis choledochi, in which case the obstructed bile may lead to dilatation of the bile-ducts and gall-badder, and to enlargement of the liver. If the occlusion is caused, on the other hand, by tough plugs of mucus which are situated in the finer (though still visible to the naked eye) hepatic ducts, as occurs in acute phosphorus-poisoning, according to the investigations of Wyss and Ebstein, the gall-bladder and the larger excretory ducts will be found empty, or almost so. The obstruction at the pars intestinalis is, however, not an absolute one, *i.e.*, it may be overcome under certain circumstances, as,

for instance, when the pressure of the bile in the ductus choledochus is correspondingly increased. The pressure of the bile, which is equal to the pressure under which it is secreted, then the action of the muscular fibres in the walls of the bile-ducts, the vigor of the movements of inspiration, perhaps also the distention of the intestines, will determine whether the bile will flow or not when the obstruction reaches a certain grade of severity. In addition, the obstruction is not always complete, *i.e.*, the pars intestinalis choledochi may be considerably narrowed, but not entirely occluded. A small portion of the secreted bile then passes into the intestines; the greater proportion, however, is retained in the larger ducts and gall-bladder. This explains the fact that the discoloration of the stools is not, by any means, always complete, and that, in other cases, the stools are at times colored, at times colorless, while the yellow discoloration of the skin barely shows any change in intensity. The gradual increase of the obstruction to the flow of bile also explains why the jaundice develops more slowly in catarrhal icterus than, for instance, in the suddenly developing occlusion of the choledochus by gall-stones. While, in the latter, the yellow color of the skin appears within six hours after the occurrence of the occlusion, and may be fully developed in twelve hours afterward, we find that three days elapse, as a general rule, in catarrhal icterus before the conjunctiva becomes yellow, and five to six days before the yellow discoloration of the skin has reached its maximum.

The pulse and temperature of the body are influenced by the jaundice, or, to speak more accurately, by the biliary acids which have passed into the blood. The rapidity of the pulse diminishes, as a rule, upon the development of icterus; if it was previously normal, it not infrequently sinks to fifty beats per minute. If fever does not happen to be present, the temperature of the body falls to 36.5° C. (97.8° F.), or even lower.

Only in very rare cases of catarrhal icterus does the saturation of the blood with ingredients of the bile reach such a height that the grave symptoms of poisoning develop which are known under the term cholæmia. If the kidneys, which must be regarded as by far the most important organs in the excretion

of the constituents of the bile which have accumulated in the blood, functionate normally, and the excretion of urine is not accidentally interrupted (for instance, by occlusion of the ureters, etc.), no symptoms of cholæmic poisoning, and especially no grave cerebral symptoms, will develop, even when the ductus choledochus is completely occluded, if this does not continue more than two to three weeks, as usually occurs in catarrhal icterus.

The local symptoms on the part of the liver and gall-bladder, viz., enlargement of the liver, pressure and painful sensations in the right hypochondrium, enlargement of the gall-bladder in the form of a tumor which is as large as a dollar, not very hard, and projects beneath the lower border of the liver, are entirely absent in numerous cases of catarrhal icterus, or are often so slight, when compared with the accuracy of our explorative measures, that they are worthless in making a diagnosis, at least from a positive point of view. They are especially absent when the catarrh does not affect the large excretory bile-ducts. If the previously mentioned local symptoms are present in their entirety, they serve to indicate positively that the catarrh involves the terminal portion of the ductus choledochus, and has led to its occlusion. The bile secreted under such circumstances will distend all the bile-ducts, including those situated within the liver, upon which depends the increase in the volume of the liver and the tension of its serous coat, which causes the patient to experience shooting pains and dull pressure in the region of the organ. These sensations are also due, in part, to the dilatation of the gall-bladder, whose serous covering has been immoderately distended. In addition to the large quantity of the bile which presses backward from the choledochus, the enlargement of the gall-bladder is, perhaps, also due to a sort of paralytic condition of its muscular coat, which we may explain by the spread of the inflammatory process from the mucous membrane.

If the catarrh is limited to the gall-bladder, no increase in the size of the liver will be noticeable. The gall-bladder also will not, as a rule, be enlarged to such an extent that it is recognizable upon palpation and percussion, but, at the most, a feeling of dull pain will be felt in the right hypochondrium, which we must regard as

due to the implication of the serous membrane in the inflammatory condition of the walls of the organ. Jaundice will be absent; under certain circumstances, slight fever will be present. The above-mentioned factors will enable us to discriminate between catarrh of the bile-ducts and isolated catarrh of the gall-bladder. Luton has thought it necessary to denote this difference by special nosological terms. To the isolated affection of the gall-bladder he applies the term cholecystitis catarrhalis, and to inflammation of the bile-ducts, angiocholitis—an incorrectly compounded word, which should be replaced by the term cholangioitis (formed in a manner analogous to that of lymphangioitis).

Complications and Sequelæ,

in the ordinary sense, occur, on the whole, very rarely in catarrhal icterus. We must especially mention the formation of gall-stones, as there can be no doubt that the catarrh, especially when it affects the gall-bladder, gives the first impetus to calculus formation, partly from the accumulation of thick mucus (rich in lime salts), partly from inspissation of the bile, which is retained in the gall-bladder, when the ductus cysticus has been occluded and rendered impermeable by the swollen mucous membrane. It goes without saying that the causal relation may also be reversed, *i.e.*, the catarrh may be due to the irritation produced by the calculus, or is, at least, maintained and increased by it. We have previously intimated that catarrh of the bile-ducts may, in individual cases, assume the character of a true blennorrhœa, continue in this manner for months, and lead to diffuse or sacculated dilatation of the bile-ducts, or even to suppuration of the latter and the formation of small hepatic abscesses. We may here mention that it appears as if simple catarrh of the bile-ducts may, in exceptional instances, be transformed into true croup. A case belonging to this category will be reported further on under croup of the bile-ducts.

Among the sequelæ of catarrh of the bile-ducts, the permanent organic occlusion of the lumen of the biliary canals is most to be apprehended. This is caused by the fact that the surfaces of the excoriated mucous membrane, which has been deprived of

its epithelium, become agglutinated at those places in which they come in contact on account of the swelling of the mucous membrane, and grow together like the granulating surfaces of a wound. Such an organic occlusion occurs, perhaps, most frequently in the relatively narrow ductus cysticus; it leads to dropsy or obliteration of the gall-bladder—symptoms which are of no special importance with regard to the subjective well-being of the patient. The occlusion of individual bile-ducts within the liver is also usually unaccompanied by any serious consequences. But the results are different when the ductus choledochus is organically and permanently occluded in the manner indicated: the bile is retained in the ducts, dilates the latter to an enormous extent, causes disappearance of the hepatic tissue, and a condition of marasmus and cachexia develops, which usually causes death after the lapse of a few months.

Diagnosis.

There can be no question of a diagnosis of simple catarrh of the bile-ducts until jaundice has developed; then, however, the recognition of the disease usually presents no further difficulties, although it still remains somewhat doubtful in the first few days, and only the further course may secure entire certainty with regard to its nature. The diagnosis of catarrhal icterus must be based upon the symptoms of gastric catarrh prior to and accompanying the jaundice, and which can be attributed, as a rule, to some definite exciting cause, such as faulty diet, a cold, etc.; furthermore, upon the usually slight general disturbance, upon the unimportance or even entire absence of changes in the liver, and, finally, upon the fact that the jaundice develops unexpectedly in individuals who are otherwise entirely healthy, and especially in the young. The simultaneous occurrence of numerous cases of jaundice, at certain times and places, is testimony to the fact that the individual case in question is one of simple catarrhal icterus. Catarrhal icterus is most readily mistaken, in the beginning, for that form of jaundice which is due to closure of the ductus choledochus and ductus cysticus by gall-stones (or by round-worms, distomata, etc.). We must, therefore, immediately endeavor to

ascertain whether the individual has not previously suffered from jaundice, combined with attacks of pain presenting the characteristics of hepatic colic, and whether gall-stones have not been observed in the stools. If this has occurred, the view that the jaundice is produced by occlusion of the bile-ducts by gall-stones would be more plausible than in the opposite case. Moreover, noteworthy differences become evident when we contrast the symptoms of catarrhal icterus with those of obstructive jaundice in consequence of the presence of gall-stones. In the icterus produced by gall-stones great tenderness is almost always present in the region of the liver, the pains occur paroxysmally, and present a cardialgic character; the icterus appears within a few hours after the paroxysm of pain, and, as has been stated above, attains considerable intensity in much less time than occurs in catarrhal icterus. The jaundice which is due to gall-stones occurs more frequently in middle and old age, and more often in the female than male sex, while catarrhal icterus especially affects the young, and more often the male sex. Rapid development and disappearance of icterus, variations in its intensity, which go hand-in-hand with paroxysms of pain, constitute testimony to the view that the jaundice is due to gall-stones. A more uniform course of the icterus, without variations in its intensity and without paroxysms of pain, and a duration of the jaundice of about three weeks, speak in favor of catarrhal icterus. The appearance or absence of biliary calculi in the fæces will, however, soon give a positive solution of this question.

Catarrhal icterus may also be mistaken, in the beginning, for that variety of jaundice which accompanies diffuse inflammations of the liver, cirrhosis, acute yellow atrophy of the liver, hepatic cancer, and various other grave affections of this organ. But in all these diseases the icterus will be preceded, as a rule, by other symptoms, in addition to those of gastric catarrh, especially on the part of the liver itself; the general condition will be more seriously affected in them, and a careful examination of the patient, which is advisable in every case of icterus, will generally show more marked changes in the liver than belong to catarrhal icterus, in which they may even be entirely absent. The uncertainty in the diagnosis will, however, only continue for a few

days, as the observation of the further course of the disease will soon show whether we have to deal with a mild, simple catarrh of the bile-ducts or with a deep-seated and dangerous affection of the liver.

Catarrhal icterus may also be mistaken for that form of jaundice which is produced by compression of the ductus choledochus or ductus hepaticus, by means of small tumors which are not recognizable by palpation, and by similar anatomical lesions. The short duration of the jaundice in simple catarrh is here decisive, as well as its chronic character when tumors are present which press upon the biliary canals. The difficulty of the differentiation increases, and the diagnosis may be undecided for months, in those cases in which the catarrh of the bile-ducts has become chronic. A decision concerning the catarrhal nature of the affection in such cases can only be arrived at when the jaundice, which together with its producing cause has been regarded as irreparable, finally disappears and perfect health is gradually restored.

Duration, Termination, Prognosis.

Ordinary cases of catarrhal icterus have a duration, on the average, of about four weeks. Milder cases, which are known as icterus simplex on account of the absence of symptoms on the part of the stomach and the very slight affection of the general condition, often run their course in a much shorter period, viz., in ten to twelve days. This occurs with special frequency in epidemic icterus. On the other hand, cases occur, though very rarely, in which the catarrhal jaundice continues much longer than usual (even three to four months), until the bile finally makes its accustomed escape into the intestines. Frerichs (l. c. p. 423) reports a case of this kind occurring in his own experience, in which, however, the general condition was scarcely more affected than in the usual shorter course of the disease. Catarrh of the bile-ducts, which accompanies diseases of the liver, varies in duration according to the nature of the primary hepatic affection. It usually disappears quite rapidly, but, on the other hand, returns with greater readiness.

The disease almost always runs a favorable course, and recovery is complete. A more infrequent termination of the catarrh is the suppurative inflammation of the bile-ducts with diffuse or sacculated dilatation of the biliary canals, which may reach such a degree of intensity that the hepatic tissue is thereby compressed and partly made to disappear, or which is accompanied by the formation of small abscess-like cavities in open communication with the dilated biliary canals. These very grave changes occur with the greatest readiness when the mouth of the ductus choledochus is permanently and organically closed by a process analogous to adhesive inflammation (cf. on this point the chapter on occlusion of the bile-ducts).

Prolonged duration of jaundice is often followed by anæmia and emaciation, even when recovery finally occurs. In unfavorable cases, in which the disease is prolonged by repeated errors of diet and irregular habits of life, such as are produced by want and privation, even the danger of cholæmic intoxication is not excluded, and this always pursues a fatal course if severe cerebral symptoms have been induced.

The prognosis in general may, therefore, be termed favorable in simple catarrhal icterus. We must not, however, omit to mention that cases are not extremely rare in which a patient, after he has merely presented for two to three weeks the symptoms of simple catarrhal icterus, and although his condition had not given rise to the faintest suspicion of danger, is suddenly affected with severe nervous symptoms and presents the signs of icterus gravis. Such patients usually die after a few (two to three) days, and the autopsy reveals the changes which are characteristic of acute yellow atrophy of the liver. If the catarrh of the bile-ducts and the icterus produced thereby is only part-symptom of some more serious disease, such as pneumonia, typhus, acute phosphorus-poisoning, etc., the prognosis will naturally depend upon the latter. If the catarrhal jaundice is undiminished after a period of four weeks, if dull pains are continually experienced in the region of the liver, if shooting pains are superadded from time to time, and variations in the intensity of the jaundice are perhaps noticeable, the prognosis becomes much more grave. These phenomena point toward a beginning

dilatation of the bile-ducts, a fact which is of bad omen, because as a rule it presupposes a permanent closure of the mouth of the ductus choledochus.

Treatment.

In the treatment of catarrhal jaundice, the etiological factors of the disease must first be taken into consideration. If the latter has begun with symptoms of gastric catarrh; if nausea, vomiting, perverted taste in the mouth, protrusion of the epigastrium and similar symptoms are present, the exhibition of an emetic is indicated, though only under the condition that the gastric catarrh has been produced by an excess of indigestible food and abnormal products of decomposition in the stomach. If this supposition does not hold good, it is better to omit the use of emetics because, when used carelessly and excessively, they very readily aggravate the catarrhal condition of the gastric mucous membrane, and the act of vomiting in itself may give rise to jaundice. During the later period of the disease emetics have also been often employed with the view of overcoming, by the act of vomiting, the obstruction which prevents the flow of bile. We shall soon return to this point. If the catarrhal icterus is attributable to a cold, in which event bronchial catarrh is often present at the same time, diaphoretic measures are indicated in the beginning. The patient should take a warm full bath, or what is perhaps still better, a vapor bath, and should secure a continuance of profuse perspiration, or he should be kept in bed, and the attempt made to produce diaphoresis by internal remedies (warm drinks, tartar-emetic in interrupted doses, etc.).

The indicatio morbi would, in the main, be satisfied in most cases of catarrhal jaundice, if we were able to remove the obstruction which opposes the flow of bile into the intestine at the pars intestinalis choledochi. The attempt to effect this object has been made in various ways: by the use of emetics, the internal administration of acids and alkalies, and finally by mechanical means, through stimulation of intestinal peristalsis by means of copious injections of cold water into the intestines, or finally, by compression and faradization of the gall-bladder.

Emetics, apart from their immediate object of emptying the stomach, are supposed, on account of the active contractions of the diaphragm and the abdominal walls which occur during the act of vomiting, to exert pressure upon the distended large bile-ducts, and in this manner to remove the obstruction at the end of the ductus choledochus. There is no doubt that sufficiently vigorous contractions during emesis will have this effect; but it will only, as a rule, be of short duration, as the obstruction consists less of the plug of mucus (although even this may soon be re-formed) than of the swelling of the mucous membrane at the narrow portion of the canal. This may be temporarily overcome by the emetic, but will not be permanently removed. We can therefore understand why some reliable observers have obtained no success in the treatment of icterus by emetics, while others praise their efficacy. On account of the powerful action of emetics upon the mucous membrane of the stomach and duodenum, however, it is advisable, as a rule, to desist from their use and employ other and less active remedies, such as acids and alkaline substances, which have long enjoyed a high repute as curative measures in jaundice. The action of acids (aqua regia, nitric and hydrochloric acids, citric acid, etc.), is explained on the theory that these remedies, by irritation of the duodenal mucous membrane at the caruncula duodenalis major, produce reflex contractions of the gall-bladder, which may increase the pressure in the ductus choledochus to such a degree as to overcome the obstruction of the pars intestinalis. Alkalies, however, which are usually administered in the form of mineral waters, act favorably upon the jaundice by increasing the secretion of bile, and therefore the pressure in the ductus choledochus, and also by increasing the power of the alkaline bile to dissolve mucus. In addition, the anti-catarrhal effects of these remedies is also beneficial to the mucous membrane of the stomach and duodenum.

Krull[1] advises the employment of large injections of cold water in the intestines in catarrhal icterus, starting from the idea that a harmless irritation of the biliary excretory ducts

[1] Berl. klin. Wochenschr., 1877, No. 12.

may be produced by increase of the peristaltic movements of the intestines, and that the obstruction which opposes the flow of bile may thus be overcome. Whether the good effects of these injections of cold water (which had been previously recommended by Mosler) depend solely upon the increased peristalsis, or whether the cold water produces, at the same time, a change in the circulatory or secretory conditions of the liver, is left undecided by Krull. His plan is as follows: when the catarrhal icterus is prolonged, or as soon as the diagnosis is rendered positive, the patient slowly receives, by means of an irrigator, an enema of cold water once in twenty-four hours. The quantity of water varies from one to two litres, at a temperature of 12° R. (59° F.); when the injections are repeatedly made, their temperature is gradually increased to 18° R. (72.5° F.), because after repeated application of the water the intestine does not tolerate the low temperature as well as before. The patient must endeavor to retain the water as long as possible. More than seven injections were never employed, as a larger number was unnecessary. Among eleven cases which were successfully treated in this manner the shortest had only lasted five days, the longest almost one and a half years. All drugs were discontinued, and ordinary diet administered. The first effect of the treatment consisted in the rapid disappearance of the pressure in the epigastrium, of which all the patients complained, of the nausea and headache, and the return of the appetite. When the disease had not lasted too long, these disturbances were dissipated in twenty-four hours, and complete recovery occurred within a few days. Even in the protracted cases this result was obtained within several days. In half the cases, fæces colored with bile were passed after the second injection; in all cases, even in those of long duration, this occurred at the latest in two to four days. A striking feature is the rapid disappearance of all gastric disturbances, which must, perhaps, be regarded rather as a symptom than as the active cause of the catarrhal icterus.

A few years ago Gerhardt (l. c.) referred to the purely mechanical treatment of catarrhal jaundice by compression and faradization of the gall-bladder. The compression of the gall-bladder is, as a matter of course, only possible when it can be

distinctly palpated, or when it causes the abdominal walls to protrude perceptibly. It should then be clasped by the fingers and emptied by pressure by forcing it against the vertebral column. "We can feel, while the gall-bladder suddenly becomes imperceptible, a fine blowing murmur, and can convince ourselves by percussion that the dulness of the gall-bladder, which had been previously demonstrable, has disappeared." The effect does not alone appear immediately—in many patients the appetite at once improves, or the pruritus of the integument disappears by the next night, and the first bile-colored stools appear on the second day—but it is usually permanent. However, Gerhardt acknowledges that the duct may again close, if the swelling of the mucous membrane continues, and that it may be necessary to repeat a similar procedure several times. We disregard the fact that manual compression of the gall-bladder is only possible in a relatively small number of cases, on account of the relations of this organ, but feel ourselves compelled to refer to the possible dangers of the manipulation. We may believe that we have to deal with simple catarrhal icterus, although ulcerations may be present at the same time in the gall-bladder, and its walls (like those of the ductus cysticus and choledochus) may present weak points, which furnish a possibility of rupture of the gall-bladder, even though the compression be cautiously performed. The danger is so much the greater, as ulcerations of the gall-bladder and larger bile-ducts quite frequently do not reveal themselves by the slightest symptom. If the gall-bladder is not accessible to the compressing finger, the requisite compression of the organ may be produced by means of electricity. Copland mentions that Hall and Darwin had employed electricity for the removal of jaundice. Gerhardt places one electrode of a strong induction current with slow interruptions in the region of the gall-bladder, and the other electrode horizontally opposite, next to the vertebral column on the right side. The effect of this method can be controlled with certainty by watching the color of the urine.

In the large majority of cases of catarrhal icterus we may remain content with expectant measures or, at least, with purely symptomatic treatment. If the general condition is perceptibly

affected, and perhaps even fever is present, the patient should keep to bed; otherwise he may remain in the open air, and moderate physical exercise should be recommended in mild weather. The diet must be carefully regulated, and should only consist of soups and light vegetable food (vegetables, preserves, etc.), especially so long as gastric symptoms are present. Cooling, acid drinks, such as soda-water, citric lemonade, etc., may also be allowed. Especial weight must be attached to regulation of the stools. The tendency to constipation, which is usually present, may be counteracted by a few doses of castor-oil, instead of which mild laxative salts (Glauber's salts, cream of tartar, sal seignette, etc.), infusion of rhubarb with bicarbonate of soda, or even small doses of aqueous extract of aloes, tincture of colocynth, and similar remedies, may be employed according to the circumstances of the case. If the stomach is more severely affected, enemata should be resorted to instead of the above-mentioned purgatives. If, on the other hand, diarrhœa occurs, a Dover's powder or other opiate, may be administered in small doses. Pains which may be present in the region of the liver are combated, when they become annoying, by warm poultices in this locality; local abstraction of blood for this purpose should be avoided. Pruritus, which is often very annoying in icterus, is relieved by washing the skin with cold water or diluted vinegar, by inunction with chloroform, etc. Frequent warm baths have a good effect in rapidly removing the icteric color of the skin, as soon as the flow of bile into the intestine has been re-established; they are also useful in relieving the pruritus. If the catarrhal icterus continues unusually long, we find that, in addition to more powerful derivation to the intestines, and the external and internal employment of empirical remedies, such as aqua regia, especially the sufficiently prolonged use of mineral-waters, notably Carlsbad, Marienbad, Vichy, Ems, Kissingen, Homburg, etc., are indicated, and so much the more when deeper-seated lesions threaten to develop in the liver in consequence of catarrh of the bile-ducts, or when the jaundice itself is maintained by hyperæmia of the liver, induration, fatty infiltration, and similar conditions. In addition to the mineral-waters mentioned above, herbs, grape-cures, the

bitter extracts, etc., may be tried in such cases. In symptomatic catarrhal icterus the treatment must chiefly take the primary disease into consideration, and only specially prominent disorders due to the icterus need to be combated symptomatically.

Purulent, Diphtheritic and Ulcerative Inflammation of the Biliary Passages.

(*Cholecystitis and Cholangitis suppurativa, diphtheritica, exulcerans—Exudative inflammation of the bile-ducts of Frerichs—Cholecystitis and Angiocholitis of the French authors.*)

Andral, Clinique médicale. 4 éd. T. II., p. 549.—*Louis*. Fièvre typhoïde. 2 éd. T. I., p. 28.—*Dance*, Arch. gén. de méd. 1828. T. XIX., p. 40.—*Rokitansky*, Handb. d. pathol. Anat. 1842. III. Bd. S. 367.—*Budd*, Die krankhten. d. Leber. German by *Henoch*. 1846, p. 175.—*Henoch*, Klinik d. Unterleibskrankheiten. I. 2 Ed. 1855, p. 79–84.—*Frerichs*, Klinik d. Leberkrankhtn. II., p. 427.—Dictionnaire encyclopédique des sciences médicales by *Dechambre*. T. IX. Paris, 1868, p. 323 et seq.—*Klebs*, Handb. d. pathol. Anat. 1869. I., p. 479.—*Huenicken*, Beobachtung einer croupoesen Gallencanal-Entzündung. Berliner klin. Wochenschr. 1870. No. 27, p. 326.—*Birch-Hirschfeld*, Lehrb. d. pathol. Anat. Leipzig, 1877, p. 964.—*C. E. E. Hoffmann*, Untersuchgn. üb. d. pathol.-anat. Veränderungen d. Organe beim Abdominaltyphus. Leipzig, 1869, p. 222.—*Ibid.*, Virch. Arch. XLII., p. 220.—*Quinquaud*, Les affections du foie. 1. fasc. Paris, 1879 (Cholangitis hemorrhagica).—*Teuffel*, Ueber eine eigenthümliche Form von Hepatitis (Hep. sequestrans). Diss. Inaug. Tübing., 1878 (Reprinted in Schmidt's Jahrb. d. ges. Med. 1878).—*P. Carl*, Ueber hepatitis sequestrans. Diss. Inaug. Tübing., 1880.

The severe forms of inflammation of the bile-ducts which are included under the above heading belong, according to the united opinion of all who have examined the subject, to a relatively slightly investigated chapter, which is still in need of study in many points. In many treatises and text-books on pathology we find that the forms of disease in question are not even treated as separate conditions; it has been deemed sufficient to refer to their rarity, and they are generally regarded as a consequence of cholelithiasis and certain parasites, or as complications of typhoid fever, etc., and are therefore incidentally discussed with these affections. There would be no objection to this if cases of suppurative inflammation and ulceration of the bile-ducts did

not occur, which are unconnected with the above-mentioned forms of disease, and which cannot be passed over in silence because they develop rarely or appear, for other reasons, to possess slight significance in practice.

On the whole, however, the inflammations of the bile-ducts under discussion do not often come under observation.

The symptoms are frequently very slightly characteristic, the disease may, despite its often ominous significance, be readily mistaken and even entirely overlooked, especially when, as usually happens, it occurs in combination with other diseases, the symptoms of which occupy the foreground and engage the entire attention of the physician. Our knowledge of suppurative inflammation of the bile-ducts and the conditions connected with it, must, therefore, be attributed in great part to observations in the dead-house, and even here it is not always possible to explain the mode of development and the intimate relations of the changes which present themselves.

Inflammations of the bile-ducts present great differences with reference to their anatomical characters. A simple catarrh, which is chiefly recognizable by the more profuse production of a mucoid secretion, may progress to inflammation with purulent or croupous exudation, even to denudation of the mucous membrane, to ulceration and gangrene of the walls of the bile-ducts, according to the intensity of the causative irritation and the vulnerability of the affected parts. It is impossible to sharply differentiate these forms which are anatomically so different, because they merely vary in degree, and not, so far as we are able to see, in their essential character. We shall only devote separate attention to croup of the bile-ducts. We could more readily endeavor to differentiate the cases according to the distribution of the inflammation over the various regions of the biliary canal system, so that we might separately consider inflammation of the gall-bladder, that of the larger excretory ducts as well as of the bile-ducts situated in the interior of the liver. With regard to the symptoms, at least, such a division follows of itself. But even in the description of the anatomo-pathological relations we cannot dispense with a separation of exudative cholecystitis from the corresponding forms of cholangitis.

Etiology.

The overwhelming majority of all cases of purulent inflammation and ulceration of the bile-ducts may be attributed to the presence of gall-stones and other foreign bodies (worms), which act as mechanical irritants to the mucous membranes with which they are in contact. Inflammation which has developed in this manner always presents, in the beginning, the anatomical appearances of simple catarrh, but the latter may, when the irritation is more intense or the individual susceptibility is increased, advance into inflammation with purulent, even croupous, exudation, and, indeed, even abrasion, ulceration, and gangrene may appear in the walls of the bile-ducts. The inflammation is then usually confined to those places, or, at least, to that tract—gall-bladder, large excretory ducts, hepatic biliary canals—which are directly subject to the irritation. It sometimes happens, however, that it spreads from the part primarily affected over larger areas, and indeed, over the entire system of bile-ducts, inasmuch as it advances along the walls of these canals. In this respect a striking disproportion is sometimes noticeable between the apparently innocent nature of the foreign body and the restricted character of the lesion directly produced by it, and the severity of the anatomical changes and their wide distribution throughout the system of bile-ducts.

Cases are observed in which the purulent cholangitis has spread over all the biliary canals within the liver, in which, perhaps, it has led to the development of numerous small hepatic abscesses, and in which, nevertheless, all these canals are found free of foreign bodies, while one or a few gall-stones are observed in the gall-bladder or large excretory ducts, although it is well known that a much larger number of exactly similar concretions are present in many other cases without an indication of cholangitis. Under such circumstances it is questionable whether we should satisfy ourselves with the presence of the foreign body in question and regard it as the sole cause of the cholangitis. We must rather attempt to determine whether other causes, to which we shall soon refer, may not have been acting, and whether

accidental mechanical influences, as, for instance, falls or blows upon the region of the liver, may not have acted in combination with the former factor in producing the widespread cholangitis. It may also occur exceptionally that the primarily affected spot, or the region in which the concretion has been observed, shows a slighter grade of inflammation than other parts to which the disorder has subsequently extended. In those cases in which the inflammation extends beyond the region which has been directly subject to the mechanical irritation we must always endeavor to decide whether the presence of the concretions may be regarded as the only cause of the affection. The possibility that a chronic inflammation of the bile-ducts may be followed by the formation of concretions, that the causal relation between the two phenomena may be entirely the reverse of that described above, must always be taken into consideration. The question may also be raised whether the inflammation of the bile-ducts which is present and the development of the concretions which are found at the same time may not be attributed to a common cause which should be sought for in an abnormal constitution of the bile itself.

Purulent cholangitis can be caused by parasites (worms) which have reached the bile-ducts by any means, in the same manner as by biliary concretions. Round worms, distomata, and echinococcus cysts have been observed in the biliary passages, and may there produce inflammations of varying intensity. However, cholangitis due to this cause is not alone rare, at least in man, but is usually of a mild form.

To a second group belong those cholecystitides and cholangitides which occur during the course of severe typhoid fever and other acute infectious diseases, such as cholera, yellow fever, pyæmia, puerperal fever, dysentery, etc. The ulcerations of the gall-bladder, observed by Blane in the fever which occurs upon Walcheren Island, and by Boyle and others in the remittent bilious fevers of tropical countries, probably also belong to this category. The inflammation in these cases is sometimes confined to the gall-bladder; sometimes it affects, in addition, or even exclusively, the larger excretory bile-ducts both within and without the liver.

The processes in question are characterized in general by the fact that they lead to necrosis and abrasion of the upper layers of the mucous membrane. The abraded layers must perhaps be regarded as diphtheritic pseudo-membranes. If the patient remains alive for a sufficiently long period, removal of the necrosed part and ulceration will occur at the place in question. This is sometimes accompanied, at least in the gall-bladder, by extensive gangrene of the walls, which become converted into a soft, easily torn mass. If adhesive peritonitis does not occur in time over the affected region, rupture or ulcerative perforation of the gall-bladder as well as of the larger bile-ducts may follow. Large cavities filled with bile, fetid matter, and the débris of tissue softened by gangrene may form in the neighborhood of the gall-bladder; these cavities are enclosed by the adjacent organs that have become adherent by inflammation, and the gall-bladder sometimes appears to have entirely disappeared. These changes of the most severe and dangerous character are, perhaps, especially observed when gall-stones happen to be present in the gall-bladder at the same time.[1] These destructive processes within the biliary passages usually continue for a longer or shorter period beyond the primary typhoid affection, and may even not appear prominently until the latter has run its course.

Various opinions have been advanced with regard to the cause of this so-called diphtheritic cholangitis in typhoid fever and allied diseases. Budd supposes that the bile, in such cases, possesses a certain acridity in consequence of the typhoid process, on account of which it must act as an especial irritant and cause of inflammation upon the mucous membrane of the biliary canals. It has been justly maintained, in opposition, especially by Frerichs, and lately by Jaccoud and others, that such a change in the bile cannot be demonstrated in typhoid fever, and that in case the bile should act as an irritant to the bile-ducts, the irritation would prove less severe in typhoid fever, because the secretion of bile in this disease is usually markedly diminished. It is much more natural to connect the secondary cholangitides—as is

[1] Cf., for instance, *C. E. E. Hoffmann*, Untersuchgn. ueb. d. path.-anat. Veränderungen. d. Organe beim Typhus abdom., Leipzig, 1869, p. 223. *Ibid.* Virch. Archiv. XLII., p. 220.

done, in the main, by Frerichs—with the low condition of the general nutrition in the infectious diseases mentioned, and which is evidenced by a certain vulnerability of the tissues as well as by a greater tendency to ulcerative degeneration and necrosis. It must, however, be conceded that in this manner we only explain the gravity and dangerous character of the process; in the present case, therefore, the tendency to ulceration and gangrene of the biliary canals which have been changed by inflammation, while the fact that merely the mucous membrane of the larger bile-ducts and the gall-bladder should become affected, together with the immediate cause of this local affection, still require an explanation.

A third group is composed of those rare cases in which neither foreign bodies nor acute infectious diseases can be regarded as the cause of the inflammation. In occlusion of the bile-ducts, especially when this is due to carcinomatous new-formations, we sometimes find a purulent inflammation of the larger bile-ducts develop, and, in a similar manner, large and deep-spreading ulcerations are also observed in cancer of the gall-bladder, even in those parts of the organ which are not affected by the carcinoma. In the first case we may presume that the obstructed bile undergoes changes, either from mere concentration or in some other unknown manner, in consequence of which it acquires a certain acridity, and acts upon the biliary canals as a source of irritation. In the second case we may regard the mixture of the carcinomatous discharge with the bile as the cause of the ulcerative cholecystitis.

Whether the more severe (exudative) forms of cholecystitis and cholangitis may also be produced by those causes which, as a rule, only give rise to catarrhal icterus, such as errors in diet, exposure to cold and wet, etc., or, in other words, whether simple catarrhal icterus may be transformed into a purulent, diphtheritic, or ulcerative inflammation of the bile-ducts, is a question of great interest, for the proper answer of which too few cases have been observed. While some authors expressly deny the possibility of the transformation of the mild catarrhal into the more severe exudative forms of cholangitis, the possibility of such a change is tacitly acknowledged by others. In my opinion,

such a transformation cannot, by any means, be denied. If an individual, who has fallen into a cold river while his body is overheated, becomes affected with marked symptoms of catarrhal icterus; if, however, this disease does not terminate in recovery even after a period of six to eight weeks, but a mild degree of icterus continues for months, with manifold disturbances on the part of the digestive tract; if fever develops, which may be interrupted by prolonged periods of apyrexia; if the patient gradually becomes emaciated, his energies disappear, and death finally occurs from exhaustion after a year or more; and if the autopsy reveals a purulent cholangitis, combined, perhaps, with a number of small hepatic abscesses connected with the inflamed bile-ducts —although no biliary calculi were or are present, although typhoid fever, or an allied disease, was not previously present, although there could be no question of a contusion of the liver, or some analogous cause—we will find ourselves compelled to assume (if we are unwilling to distort the facts) that the purulent cholangitis has developed from the simple catarrhal icterus which was primarily present and due to the exposure.

Certain cases of cholecystitis and cholangitis are significant of an extension of inflammation. Inflammations of the hepatic tissue, with abscess-formation, can spread to the bile-ducts of the liver, and thus give rise to a purulent cholangitis which is at first circumscribed, and then becomes diffuse. (As a rule, however, the course of the disease is the reverse.) In the same manner suppurative pylephlebitis sometimes extends to adjacent bile-ducts. Cholecystitis due to such an extension of the inflammation can, however, occur very rarely in the gall-bladder. External injuries, contusions, and traumata in the region of the liver have also been regarded, in rare cases, as the causes of purulent inflammation of the bile-ducts. Contusions can, however, only be considered as subordinate causes, because gall-stones, or the signs of previous cholelithiasis, were always present in the cases in question. There is no doubt that wounds of the bile-ducts[1] are sometimes, though not by any means always, followed by a phlegmon of these parts, and the gravity of these wounds does

[1] Cf. *L. Mayer*, Die Wunden, etc., der Leber, Munich, 1872.

not depend so much upon the latter as (at least according to the prevailing opinion) upon the possible escape of bile into the cavity of the peritoneum.

Finally, a few cases of primary cholangitis and cholecystitis of the severe type remain, the development of which can be attributed to none of the above-mentioned causes, but which are involved in complete obscurity with regard to their etiological relations, and must, therefore, be considered, for the present, as spontaneous cholangitis, as, for instance, Quinquaud's remarkable case (l. c., vide farther on).

Purulent cholecystitis and cholangitis is chiefly a disease of mature age. Youthful individuals are comparatively rarely affected, and the period from the age of childhood until the beginning of puberty remains entirely exempt. This depends upon the presence of the primary diseases leading to cholangitis in the periods of life in question, especially upon the fact that cholelithiasis, which gives rise to cholecystitis more frequently than all other diseases, is only exceptionally observed before the age of thirty. For the same reason the inflammations of the biliary canals in question, especially those of the gall-bladder, will more frequently develop in the female than in the male sex.

Vidal (1854) observed compression of the cystic duct by an enlarged lymphatic gland, in a child seven years old. The mucous membrane of the gall-bladder was thinned, granular, ulcerated, and destroyed in many parts, so that the peritoneum alone formed the wall of the organ.

Pathological Anatomy.

In the severe forms of inflammation of the gall-bladder, the latter, at the autopsy, is sometimes found free, sometimes more or less dilated and firmly adherent to the neighboring parts by fibrous adhesions. The organ sometimes presents the usual dimensions; as a rule, however, it is dilated, and sometimes even very markedly, so that the fundus projects beyond the border of the liver as a hemispherical tumor of the size of a fist. The contents of the gall-bladder consist, in general, of a mixture of bile, mucus, pus, or ichor, in which, according to circumstances, biliary calculi of varying numbers and constitution are floating. Its

contents are sometimes almost pure pus, with which scarcely perceptible traces of bile are mixed ; in other cases, on the contrary, it is a dirty grayish green, opaque, very viscid and stringy fluid, containing whitish yellow flocculi ; sometimes, finally, it is an ichorous, thin fluid of opaque character and dirty gray color, which may also present a bad gangrenous odor. After carefully washing out its contents, the wall of the gall-bladder, especially the mucous membrane, appears in a condition of inflammatory swelling and thickening. The appearance of the mucous membrane, however, varies considerably. In many cases it is found to be generally reddened, injected, or strewn with small ecchymoses, while in other cases it is pale or gray to blackish, and pigmented diffusely or in spots. The surface of the mucous membrane may be entirely intact, *i.e.*, free from any deposit of exudation and from ulceration ; it may also, however, present all those changes usually observed in croupous and diphtheritic inflammations. In the latter event certain parts of the surface appear coated with a whitish gray croup-like false membrane, which is firmly adherent to its base or may be lifted up in larger masses. We more frequently find a diphtheritic process than a croupous inflammation upon the mucous membrane. The latter then always appears intensely reddened, its tissue is infiltrated with hemorrhages, its upper layers have undergone necrosis and have been transformed into a brownish scab-like mass, which is usually spoken of as a diphtheritic false membrane. After removal of the fresh detritus an ulcer remains, which in time may increase in area and especially in depth. At times only a single ulcer of this kind, at others, several are present ; occasionally, indeed, the larger portion of the mucous membrane of the gall-bladder is broken up by ulcerations and entirely destroyed. The size of the ulcers varies from that of a grain of hemp or a small pea to about that of a half mark. Larger losses of substance arise from confluence of the ulcers. They are generally situated at the fundus of the gall-bladder, upon that portion which is covered with peritoneum, that is, in the position in which gall-stones which may be present are usually found. However, the ulcers may also, though more rarely, be found in any other portion of the gall-bladder.

In one case under my observation, in a woman, forty-five years of age, suffering from numerous carcinomatous growths in the liver, a large nodule had proliferated into the gall-bladder and had there undergone superficial ulceration. The gall-bladder was almost as large as a fist, projected 6–7 ctm. beyond the border of the liver and contained a grayish, opaque, ichorous fluid, together with some small, round, smooth calculi. Upon the inner surface of the organ and distributed uniformly over its entire extent from the neck to the fundus, several dozen ulcers were observed, from the size of the head of a pin to about a square inch in area. The smaller ulcers were round, with smooth edges, the larger were irregularly notched, and had evidently developed from the confluence of several smaller ones. The smaller ones extended to the muscular coat, in the larger ones this was also destroyed; the base was covered with gangrenous shreds of tissue, and was merely composed of the necrotic serous membrane, which was ripe for perforation. Externally, fresh peritoneal adhesions and deposits of fibrin were observed. The edges of almost all the ulcers were undermined. The smallest ones created the impression as if they had developed from submucous abscesses, above which the mucous membrane had ruptured, as relatively large submucous spaces filled with ichor were entered through punctate or fissured holes in the mucous membrane. Closed abscesses were, however, not discovered. In some places the mucous membrane between the ulcers, especially in the neighborhood of the carcinoma, was coated with detachable grayish yellow layers of exudation (fibrin). The ductus cysticus was compressed by several carcinomatous glands, its mucous membrane, together with that of the gall-bladder itself, presented no trace of bile-staining.

Moreover, the catarrh produced by gall-stones may directly lead to excoriation and ulceration of the mucous membrane, without the previous development of a scab-formation.

The further course of ulcers of the gall-bladder which have been produced by gall-stones and other foreign bodies (worms) will be considered in the section devoted to cholelithiasis, etc. We must emphasize, however, with regard to the ulcers due to other causes, that they usually, in accordance with the nature of these causes, pursue an acute course and that they, therefore, lead to perforation and a fatal escape of bile into the peritoneal cavity with comparative frequency. It is not improbable that the ulcers which arise in consequence of typhoid fevers and similar causes, sometimes heal, but this cannot be demonstrated positively, because the traces (cicatrices) which remain may have had their origin in other processes (perhaps previously existing calculi), and because the diagnosis of ulceration cannot be made with certainty if recovery occurs.

The great tendency of the walls of the gall-bladder to gangrene in the situation of the ulcers is worthy of note with regard to ulcers of this organ (which we not infrequently find coated with an orange-colored layer of crystals of bilirubin). When ulcers of the mucous membrane are present, the muscular and serous coats of the gall-bladder are especially liable to necrosis and transformation into a soft and very readily torn, dirty brown, greasy, pasty scurf. The ulcers often lead, therefore, to perforation of the gall-bladder, to escape of its contents into the peritoneal cavity, and to rapidly fatal peritonitis or, in favorable cases, to encapsulation of the escaped contents between the layers of the peritoneum which have become adherent by inflammation; this leads to the development of irregular and often very extensive cavities filled with bile, pus, and ichor, and which, at a later period, may perforate in various directions into the intestines, externally through the abdominal walls, and even through the diaphragm into the mediastinum, bronchi,[1] etc.

In rare cases the mucous membrane of the gall-bladder is found separated from its base by suppuration and gangrene of the submucous cellular tissue over a large area, so that the necrotic mucous membrane, which is only adherent by a pedicle, floats in the fluid-contents of the gall-bladder.

Hoffmann[2] saw two cases of separation of the mucous membrane of the gall-bladder in consequence of the formation of ulcers. In one case the entire mucous membrane of the organ was separated and floating as a ragged membrane (which was only slightly adherent at the fundus) in the markedly dilated gall-bladder which was filled with mucoid gall, and the walls of which were only formed by the serous coat and the subserous tissue. In the second case, the mucous membrane was only detached over a small space in the vicinity of an ulcer, while the submucous tissue, on the other hand, was markedly infiltrated with a greenish yellow fluid over a large area. These cases occurred in patients suffering from typhoid fever, but the presence of biliary calculi in both enables

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[1] *Simmons*, Communication of a Biliary Abscess with the Right Bronchus (Americ. Journ. of Med. Sciences. No. 148. Oct. 1877, and Dtsch. Ztschr. f. pract. Med. 1878. No. 12).

[2] *C. E. E. Hoffmann*, Untersuchgn. ueb. d. pathol.-anat. Veränderungen beim Typh. abdom. Leipzig, 1869. *Ibid.* Ulcerös-brandige Zerstörung d. Gallenblase, etc. Virch. Arch. XLII., 2, p. 220.

us so much the more readily to attribute the development of the changes which have been described to the latter, as a calculus was found firmly imbedded in one case.

Ulcers of the gall-bladder have also been observed which present the greatest similarity to perforating ulcers of the stomach and duodenum. Aufrecht,[1] who lately described a perforating ulcer of the gall-bladder, appears to presuppose for them a similar pathogenesis to that of the round gastric ulcer, except that the bile must here adopt the part which is played by the acid gastric juice in the development of the latter. In suppurative cholecystitis the pus, which is formed in large quantity, may be retained in the gall-bladder so that the latter is converted into a large pus-holding sac. This so-called empyema of the gall-bladder is almost always due to the irritation of biliary calculi upon the mucous membrane of the organ, and especially occurs when the ductus cysticus has become impermeable from incarcerated gall-stones, cicatrices of ulcers, adhesive cholangitis, etc. Such cases of, at times, enormous enlargement of the gall-bladder present, during life, the symptomatology of the so-called biliary tumor. They will receive special consideration in the chapter upon dilatation of the gall-bladder (*vide* farther on).

In rare cases the wall of this organ has been found uniformly infiltrated with pus throughout its entire thickness. It also happens that small abscesses form in it which sometimes project toward the mucous membrane, sometimes toward the serous coat. It is not impossible that such abscesses may open into the gall-bladder and thus act as the starting-point for the formation of ulcers. In very rare cases the cellular tissue, which connects the gall-bladder with the liver, is infiltrated with pus—a condition which may be compared to perityphlitis. Lebert found, in a phthisical subject, the gall-bladder filled with calculi and firmly contracted upon them; it was surrounded by pus on all sides, although the suppuration was unconnected with the interior of the organ.

Phlegmonous inflammation of the gall-bladder does not always reach such a grade of intensity as to lead to suppuration.

[1] Deutsche medicin. Wochenschrift. 1879. No. 35, p. 453.

Quite frequently the inflammation is merely chronic and only leads to hyperplasia of connective tissue and fibrous thickening of the walls of the gall-bladder, which is usually followed, at a later period, by contraction and even entire obliteration of the organ. The latter, then, merely constitutes a thick-walled sac barely as large as a nut, or a hard cord as thick as the little finger, the cavity of which contains a small amount of tough mucus. This process does not lead to any disturbing effects in the individual in question, and has indeed no practical significance. This is also true of the calcification and partial ossification of the walls of the gall-bladder, in which the organ is converted into a rigid sac, like a sclerosed and calcified artery. Simple atrophy, as well as calcification of the gall-bladder, is indeed observed, as a rule, when calculi are present at the same time, but both conditions have also been noticed in cases in which no concretions were found in the gall-bladder.

In purulent inflammation of the gall-ducts the latter are somewhat dilated, and either filled with pure pus or with a viscid, grayish green mixture of pus and bile. This change is observed in the large excretory ducts as well as in the bile-ducts situated within the liver; it may occur alone, *i.e.*, without simultaneous inflammation of the gall-bladder, but may also be combined with purulent cholecystitis. The mucous membrane of the larger excretory ducts appears swollen, flaccid, excoriated, or even covered with superficial ulcerations of variable dimensions. The congestion, which was primarily present, has disappeared, as a rule, when the autopsy is made, and the mucous membrane presents a blanched, pale gray, or slate gray color. Further changes, which are recognizable by the naked eye, may be absent, but sometimes the wall of the excretory ducts, together with the surrounding cellular tissue of Glisson's capsule, is infiltrated with pus, and the inflammation then readily spreads to the adjacent portal vein and its branches, *i.e.*, purulent pylephlebitis develops. The formation of ulcers in the large excretory ducts rarely occurs except in cases in which the inflammation is due to gall-stones; in extremely rare instances, however, the cholangitis which appears in the course of typhoid fever leads to the development of ulcers, and while ulcerative perforations

of the excretory ducts in consequence of calculi are observed with comparative frequency, perforations from other causes must be regarded as extreme rarities.[1]

In the finer bile-ducts which are situated within the liver, the changes are often not restricted to filling of the canals with pus and greater or less distention caused thereby, but their thin walls have broken down in numerous places and the suppuration has spread to the surrounding hepatic tissue. We find in such cases, the development of which is almost always due to the presence of calculi, that the liver is infiltrated with a large number, sometimes with many hundred, abscess-like cavities, which rarely exceed the size of a pea, though they may sometimes, especially by the confluence of smaller cavities, attain the size of a hen's egg. These cavities contain a thick, yellowish green mass, consisting of bile and inspissated pus, with which small, soft biliary calculi are often mixed. They are termed biliary abscesses on account of their contents, in contradistinction to the ordinary idiopathic hepatic abscesses. The small abscesses are originally surrounded by jagged, softened hepatic tissue, but at a later period they appear to be more sharply defined, and surrounded by a fibrous capsule. This process has been not inaptly likened to the formation of pulmonary cavities which are due to purulent peribronchitis. The hepatic tissue, in so far as it is unaffected by ulceration, appears in such cases of an intense icteric hue, and is found in a condition of parenchymatous or even granular degeneration.

It has been generally believed hitherto, with regard to the development of abscesses in consequence of cholangitis, that the purulent infiltration of the walls of the bile-ducts has extended to the surrounding hepatic tissue. It appears, however, that there is still another mode of development of these abscesses, especially in those cases in which numerous minute ones are scattered through the liver. According to the investigations of Rob. Teuffel,[2] which were carried on under my supervision upon the liver of a woman suffering from cholangitis calculosa, such abscesses may also arise independently of the bile-ducts. A marked infiltration, we may even say incrustration, of a small part of the hepatic

[1] Cf. Andral's case in his Clinique médic. IV., p. 495.

[2] Ueber eine eigenthümliche Form von Hepatitis (Hep. sequestrans). Dissert. inaug. Tübingen, 1878.

tissue occurs first with constituents of the bile, especially with brown pigment. The part incrusted with bile appears to undergo necrosis; a reactive inflammation develops around it, during which it is surrounded by a broad zone infiltrated with pus, which finally softens. The brown spot is thus entirely separated from its surroundings, and remains in the cavity of the abscess as a firm, slightly moist plug, which presents the appearance of a gall-stone of the consistence of thick porridge. In the case described by R. Teuffel, similar biliary, firm plugs could be extracted from all the abscesses (which were often only as large as a pea), and for which a more satisfactory explanation could with difficulty be found, as the hepatic cells contained in them could with certainty be recognized as such. As a matter of course, these abscesses may, at a later period, enter into open communication with bile-ducts; this is not a necessary consequence, however, but merely occurs accidentally. R. Teuffel has applied to the process just described the term hepatitis sequestrans. We might, perhaps, with more propriety call it furunculosis hepatis.

I was recently able to satisfy myself of the correctness of the above views in a case of mild cholangitis calculosa.[1] Abscess-formation had only occurred in a few spots, only the inception of purulent hepatitis was observed, and Glisson's capsule around the inflamed portions of the bile-ducts was diffusely infiltrated with pus, though not softened. On the other hand, numerous brown to greenish spots of about the size of a mustard seed, and which were in part sharply circumscribed, were found in the parenchyma of the liver. I looked upon the smaller spots, at the autopsy, as transverse sections of bile-ducts with inspissated contents, others reminded me more of so-called bile-duct tuberculosis. Microscopical examination of these bile-stained spots taught me, however, that they were unconnected with bile-ducts, but that I had to deal with small spots of hepatic tissue, which were impregnated to the highest extent with bile-pigment, and in the neighborhood of which reactive inflammation and purulent demarcation had already begun. We evidently had to deal with the initial stage of those small hepatic abscesses which are filled with firm biliary plugs. I have hitherto been unable to obtain any information with regard to the process of incrustation of the hepatic tissue with biliary coloring matter, the exciting cause thereof, and other similar questions.

When abscess-formation occurs in the liver in consequence of cholangitis, numerous small abscesses, as a rule, develop. However, cases have also been known, in which very large abscesses have formed—10 ctm. in diameter (Schuetzenberger), and even as large as a child's head (Frerichs). Such large abscesses are usually found singly, and the connection of their cavities with the lumen of one of the larger bile-ducts, which had been de-

[1] Cf. *Carl*, Ueber Hepatitis sequestrans. Dissert. inaug. Tübingen, 1880.

stroyed, could be demonstrated with perfect certainty, as in Klebs' case, in which a single biliary abscess as large as a hen's egg developed as a sequel of typhoid fever.

Milder phlegmonous inflammations also occur in the bile-ducts within the liver as well as outside. They lead to a connective-tissue thickening of the walls of these canals, which are also usually found filled with calculi and diffusely dilated, or provided with irregular pouches corresponding to the individual concretions. The hyperplasia of the connective tissue may spread from the bile-ducts to the interlobular connective tissue of the liver, and either lead to widespread cirrhotic changes or to circumscribed atrophy, and even to entire disappearance of the hepatic tissue between the degenerated bile-ducts.

We must mention as a rare occurrence, which, however, does not possess any practical importance, that chronic phlegmonous cholangitis may terminate in calcification and partial ossification of the walls of the bile-ducts—a process which, as is well known, has been observed quite frequently in the gall-bladder. Soemmering and Hufeland have observed and described this change in the ductus choledochus.

In the rare cases of *croupous inflammation* of the bile-ducts, succulent whitish, tubular membranes of fibrin are observed in them, exactly similar to those found in croup of the bronchi, which extend with uniform thickness over the mucous membrane of the ducts (these are sometimes unchanged, sometimes reddened and flaccid), and can be readily removed from their base. Rokitansky (l. c.) found these croup-tubes filled with inspissated bile in the form of branching concretions, by which the biliary canals were closed in the distribution of the croup and the ducts situated farther back were dilated. In the so-called *diphtheritic inflammation* of the bile-ducts, the mucous membrane, which has been usually irritated by foreign bodies, becomes necrotic in its superficial layers, and is transformed into a brownish, soft, and moist scurf which can be readily detached. Ulcerative perforation or rupture of the bile-ducts may supervene upon this process, or, in favorable cases, cicatrization of the ulcer, and finally stenosis of the duct, after the necrotic masses of tissue have been removed. As a rule, however, such cases will pursue a

fatal course, even before the secondary changes, to which we have referred, have developed.

Symptoms.

Exudative inflammation of the bile-ducts may run its course entirely without symptoms; frequently its presence is not indicated by any symptoms during life, and the autopsy alone reveals the changes which are present. This is especially true of the inflammations of these organs which develop during the course of typhoid diseases. The severe symptoms of typhoid fever mask the slight disorders which may be present on the part of the bile-ducts. A similar statement may be made with regard to most affections of the biliary organs which are connected with ulceration and gangrene, irrespective of their producing cause, but under the presupposition that the inflammatory process with its sequences has not yet extended beyond the walls of the bile-ducts. More definite symptoms only make their appearance, as a rule, when the bile-ducts are either closed and stasis of bile has therefore developed, or when the inflammatory process with its consequences has spread to the adjacent organs and tissues, a condition which is often followed by the most dangerous results. Among the latter the more important are the extension of the cholecystitis to the peritoneum and the perforation of the gall-bladder into the peritoneal cavity, the formation of biliary fistulæ, which permit the escape of the bile into the pyloric portion of the stomach, the transverse colon, or externally through the abdominal walls, the extension of the cholangitis to the parenchyma of the liver (suppurative hepatitis), as well as to the portal vein and its branches (purulent pylephlebitis). The chronic cholangitis, which consists in fibrous thickening of the walls of the canals, may prove the starting-point for stricture and occlusion of the biliary ducts. However, the symptoms depend, in great measure, apart from the nature of the anatomo-pathological process, upon the situation, and also upon the extension of the inflammation along the various parts of the system of biliary canals.

Cholecystitis usually causes the patient a feeling of pressure

and dull pain, which is situated at first in the region of the gall-bladder, but may spread from this part over the entire right hypochondrium. If the inflammation extends to the serous coat of the gall-bladder, the pains will become more severe, and can be more sharply localized.

Objective symptoms may be entirely absent. Under certain circumstances we are able to show by palpation as well as percussion that the gall-bladder is enlarged. At times the gall-bladder (dilated by pus and bile) is felt at the margin of the liver as a pear-shaped or rounded, movable tumor, which is sensitive to the touch. But the organ will only be found enlarged when the ductus cysticus is either impervious, or when the former is unable to contract on account of the implication of its muscular coat in the inflammation, and is therefore passively dilated by the accumulating secretion. If this is not so, the pus which is formed in the gall-bladder will escape by the natural passage into the intestine, and therefore not give rise to any appreciable enlargement of the organ.

Hemorrhages are a rare symptom in the ulcerative form of cholecystitis, and if they become at all noticeable, must be of a very profuse character. Budd observed a case of this kind in which the large quantities of blood which appeared in the stools might have given rise to the suspicion of a gastric ulcer. It is evident that this symptom, apart from its rarity, can hardly be useful in diagnosis.

Among the general symptoms in cholecystitis we may mention fever. Slight chilly sensations, or even well-marked chills, are observed, and these may be repeated at irregular intervals for a long time. The increase in the temperature of the body, apart from the chills, usually remains within moderate limits, and, in general, the febrile movement in the conditions under consideration present a more subacute character. But fever may also be absent, and this is especially true of ulcerative changes which are combined with gangrene of the wall of the gall-bladder. When fever is present, it will be quite often impossible to attribute it, with any degree of certainty, to the cholecystitis.

In many cases the cholecystitis only discloses its presence

when local peritonitis in the region of the gall-bladder or the alarming symptoms of perforation of the peritoneum develop.

Exudative inflammation of the ductus choledochus and the hepatic bile-ducts presents symptoms similar to those of catarrh of these parts. As a rule, the inflammatory swelling of the walls and the distention of the ducts by masses of exudation will make them more or less impervious, and will therefore cause stasis, or, at least, impeded flow of the bile. The icterus developing in this manner, will, at the most, be only distinguishable from the ordinary forms of simple catarrhal jaundice by its longer duration and greater persistency. In a certain sense, however, icterus is not a constant symptom of exudative cholangitis. Although it does not often happen that jaundice is absent as a symptom in every stage of the course of pronounced cases of these diseases, nevertheless, it will often be noticed that the jaundice only develops occasionally, and disappears at other times, although no marked change has been observed in the general condition of the patient. Persistent jaundice continues, indeed, in many cases, but it only attains slight intensity; the conjunctiva and skin show a very faint yellowish discoloration, while the fæces, although paler than normal, are still found to contain bile. Entire retention of bile will probably only occur, as a rule, in the most severe forms of exudative cholangitis.

Swelling of the liver, which may, however, remain very slight, and pains in the region of this organ, which undergo exacerbations and remissions at times, constitute further symptoms. These signs also, especially the pains, will, as a rule, be more prominent in true cholangitis than in simple catarrh of the bile-ducts; but they form no grounds for the certain differentiation of the severer forms of cholangitis from the last-mentioned condition.

Finally, the fever must be taken into consideration. This is, indeed, not absent in any case during the entire course of the disease, but may only be slightly indicated at times, or may, perhaps, give way to complete apyrexia for a certain period, and then appear more prominently at other times. As soon as ulceration occurs, when abscesses form in the liver, or when the inflammatory condition extends to the portal vein, chilly sensa-

tions or true chills develop, which are repeated at irregular intervals, and are followed by a great increase in the temperature of the body and severe disturbance of the general condition. The fever and chills may continue for months, occurring sometimes with greater, sometimes with less severity. Emaciation gradually develops, the physical powers diminish, and death finally occurs from exhaustion, or, in rare cases, convalescence sets in.

Diagnosis.

It is evident from the description of the symptoms that a diagnosis of the diseased conditions in question is very difficult. In general, we may assume that acute cholangitis is probably present when pain and swelling are observed in the region of the liver, with repeated irregular chills, rise of temperature, and the other symptoms of febrile movement, in a patient who is jaundiced, and concerning whom we know, or have, at least, good cause to believe, that he is suffering from gall-stones. However, Frerichs aptly remarks that chills alone, *i.e.*, without simultaneous elevation of temperature, are not sufficient to justify the diagnosis of suppurative cholangitis and hepatitis, since gall-stones may cause chills in the same manner that they occur in catheterization of the urethra. If the symptoms just mentioned occur with free intervals of longer or shorter duration, but with progressive deterioration of the general condition, we must be suspicious of chronic cholangitis. There is, however, no doubt that inflammation of the bile-ducts may remain entirely latent for a long time, and that it is not revealed in certain cases until the symptoms of peritonitis due to perforation, of purulent pylephlebitis, etc., suddenly develop—a change in the course of the disease, the cause of which is often determined with difficulty.

When the gall-bladder is sufficiently dilated and accessible by palpation, the cholecystitis may, under certain circumstances, be recognized by the local symptoms when these have reached a considerable intensity. As a rule, however, it is rather the accompanying inflammation of the serous covering of the gall-bladder, the pericholecystitis, which can be diagnosed, as the

inflammatory and ulcerative changes in the mucous membrane of the organ are not directly noticeable. But if the local peritonitis can be attributed to the region of the gall-bladder, and if icterus is present, in addition, the diagnosis of cholecystitis is extremely probable. Hardly a doubt remains, if the more severe symptoms of peritoneal perforation are superadded.

Duration and Course. Terminations.

The duration of the disease only extends at times over a number of days or a few weeks ; its course is therefore an acute one (as, for instance, in typhoid cholangitis), or (and this is the rule) the affection pursues a more chronic, or, at least, a subacute course, and continues for several months, sometimes, indeed, for several years, especially when it is due to the irritation of calculi.

Cholecystitis and cholangitis undoubtedly terminate very often in recovery, and many physicians, indeed (Budd among others), regard this result as the rule. We will be inclined to agree with them if we reflect that the disease occurs quite often with scarcely any symptoms, and may therefore be very easily overlooked. As a matter of course, however, these remarks will apply to the milder cases, which from their very nature present the greatest chances of recovery. Recovery occurs (after the cause of the disease, for instance, gall-stones, has disappeared) by the removal of the fluid or semifluid products of inflammation (pus, fibrinous exudation, necrotic shreds of tissue, etc.) into the intestine, in the same manner that severe inflammations of mucous membranes generally recover, *i.e.*, by granulation, cicatrization, regeneration of the epithelium, etc. That even deep-seated and extensive ulcerations may recover spontaneously is shown by large cicatrices in the mucous membrane of the gall-bladder, which extend even to the serous membrane, and upon which we stumble so frequently and unexpectedly in the performance of autopsies, and by the obliteration of the bile-ducts, especially the ductus cysticus, which are observed with equal frequency.

A fatal termination is, perhaps, the rule in those cases which

can be diagnosed. It occurs, after a longer or shorter duration of the disease, in various ways, sometimes suddenly, sometimes very gradually. Some patients die from peritonitis in consequence of perforation or rupture of the bile-ducts; others from extension of the inflammation to adjacent veins, *i.e.*, from pylephlebitis,[1] or from purulent hepatitis. Or death is caused by the hectic fever, which is caused by the suppuration and the ulcerative destruction of the bile-ducts; or, finally, it is simply due to the gradually increasing exhaustion of the entire body.

If we disregard the complications and other sequences of cholangitis previously mentioned, we are unable to state that it gives rise to other true sequelæ. In a woman, æt. forty years, who was suffering from chronic cholangitis calculosa, I saw, in consequence of this disease, the development of waxy degeneration of the liver, spleen, and intestinal mucous membrane, which attained considerable intensity. I have nowhere been able to find cholangitis mentioned among the causes of amyloid degeneration.

Prognosis.

If we reflect upon the serious accidents, to which the severe forms of cholecystitis and cholangitis so often give rise, viz., ulceration, perforation, and rupture of the gall-bladder and bile-ducts, hepatic abscesses, hemorrhages, purulent pylephlebitis, etc., and upon the more remote consequences of cholangitis, such as obliteration of the ductus cysticus and ductus choledochus and its consequences, we must confess that the prognosis of these conditions must, in general, be regarded as unfavorable and even very grave. In cholecystitis the prognosis must be especially

[1] *Dance* (Arch. génér. de méd., 1829) had already described a case of pylephlebitis which was due to a cholangitis starting from the ductus choledochus. *Monod* and *Robert* (Bulletin de la soc. anat., 1828) saw phlebitis of the superior mesenteric vein develop from extension of inflammation and ulceration of the ductus choledochus to the vein mentioned. *Luys* (Bull. de la soc. anat., 1857) saw purulent pylephlebitis of the trunk and branches of the portal vein, in consequence of general suppurative cholangitis. Two more cases of pylephlebitis from the same cause are mentioned by *Frerichs* (from Lebert and Budd). In the most recent times we must mention, among other observations, that of *Quénu* (Pylephlebitis from Gall-stones, Gaz. méd. de Paris, 1878, Nos. 51 and 52).

reserved, although well-authenticated examples of recovery are not wanting, even in cases of gravity. The most trifling exciting cause, especially mechanical injuries which affect the region of the liver, may lead to the most dangerous consequences and even to a sudden fatal termination, as Cruveilhier had already brought prominently forward.

Treatment.

The object of treatment consists in the limitation of the inflammatory process, as the causal indication cannot be met in the conditions in question. Local and general antiphlogosis (naturally with a strict regard to the individual peculiarities of each case) must be resorted to: local abstraction of blood, which can be effected by leeches or cups in the region of the liver, or by leeches applied in the neighborhood of the anus; cautious inunctions with mercurial ointment or belladonna liniment upon the skin over the right hypochondrium; warm poultices or an ice-bag over the situation of the gall-bladder, according to the inclination of the patient; internally, the administration of light saline cathartics, with a vegetable diet. The greatest caution must be exercised if the peritoneum appears affected. The patient must then remain absolutely quiet on the back, all pressure or blows upon the region of the liver, flexion of the trunk, straining at stool, etc., must be carefully avoided, even the medical examination of the affected parts must be performed with the greatest care and gentleness. We should, therefore, avoid active remedies as, for instance, emetics, and resort rather, in addition to the previously mentioned antiphlogistic measures, to opiates which, under certain circumstances, may even be administered in large doses. In short, the treatment should be the same as that demanded in peritonitis from perforation. If, on the other hand, the disease is prolonged and the local disturbances fall into the background, irritative applications to the right hypochondrium, such as mustard plasters or repeated flying-blisters, are, on the contrary, indicated. In addition, the milder alkaline mineral-waters of Carlsbad, Ems, the Eger salt springs, and similar waters should be methodically employed, and symptomatic

treatment in other respects should be adopted. If the fever of suppuration develops, and chills occur, we must employ a strengthening but non-irritating diet, and give quinine in the requisite large doses, in addition to other tonic measures. If the chills and fever are due to cholecystitis, the eventuality of an operative procedure[1] may be taken into serious consideration, especially when the gall-bladder is considerably enlarged.

Croup of the Biliary Passages.

(*Cholecystitis and Cholangioitis crouposa.*)

Rokitansky, Handb. d. pathol. Anat. 1842. III. Bd. S. 367.—*Huenicken*, Beobachtung einer croupösen Gallencanal-Entzündung. Berl. klin. Wochenschr. 1870. No. 27, S. 326.

We are well aware that we are perhaps adopting an artificial division, when we consider croupous inflammation of the bile-ducts separately from the exudative inflammatory processes previously described. We are led to do this by purely extrinsic reasons, as it appears advantageous to shed a certain amount of light upon the field of exudative cholangioitis (which includes so many different conditions) by provisorily separating one form or the other, which is more complete in itself, from this category and discussing it apart.

A croupous inflammatory process in the biliary passages is, on the whole, a rare occurrence. As a rule, it is restricted in its position, sometimes to the mucous membrane of the gall-bladder, sometimes to spots in the large biliary canals within or without the liver; it is usually produced by the presence of foreign bodies, especially gall-stones, and must, therefore, not be regarded as a specific form of inflammation, but rather as an intensified catarrhal affection. In these cases, also, the croup does not appear in its pure form, for, in addition to the whitish yellow fibrinous layers, which adhere to the congested mucous membrane at the more irritated spots, we see in other places the appearances of a severe catarrh, with profuse produc-

[1] Cf. the remarks on cholecystotomy in the later paragraph on the treatment of "dilatation of the gall-bladder."

tion of mucus and pus over a greater or less area, and, on the other hand, the inflammation develops, in spots, into the diphtheritic form; firmly adherent fibrinous false membranes of grayish to brownish green color appear upon parts of the mucous membrane infiltrated with hemorrhages, while at the same time ulcerative lesions are present in the neighborhood or are, at least, in process of development. These cases of severe catarrh due to foreign bodies, concerning which we shall speak later in discussing cholelithiasis, are entirely analogous to the various inflammatory processes, for instance, of the mucous membrane of the bladder when calculi are present, in which also all grades of catarrh are met with in addition to croup, diphtheria, suppuration, detritus-formation, and ulceration. But although these cases are more frequent, we have less reference to them when speaking of croup of the biliary passages, than to those very rare forms which are known to but few physicians from personal observation, in which an inflammation is found in the bile-ducts, especially those inside of the liver, entirely analogous to typical croup of the respiratory passages. The croupous process is not restricted locally, but is quite uniformly distributed over all the larger bile-ducts. It manifests itself by the formation of whitish, succulent, fibrinous membranes of a tubular form, which cover the reddened mucous membrane of the bile-ducts (which is also infiltrated with serum) in a uniform thickness, and can be readily detached from their base. Rokitansky found these croup-tubes filled with inspissated bile in the form of branching concretions, by which the bile-ducts are occluded in the region of the croup, and those situated farther back are dilated. This pure form of croupous cholangitis is observed in the course of severe infectious diseases, typhoid fever, cholera-typhoid, pyæmia, etc.

From a pathogenetic point of view it is not clearly settled whether the croup in these cases should also be regarded as an intensified catarrh of the bile-ducts.

Perhaps this is an inflammation due to a specific cause, only that we are not acquainted with the infectious substance which gives rise to it, and it is also doubtful whether it enters the mucous membrane of the bile-ducts from the intestines or the blood; perhaps it is only an abnormally constituted bile, or a sort of for-

eign admixture of the latter, which acts as an excitant of inflammation upon the mucous membrane of the ducts. However, this severe disease has never, as it appears, been hitherto recognized in the living subject, but it has always been found accidentally during autopsies. The disease, therefore, produces no symptoms, or the latter are not sufficiently characteristic and are too thoroughly concealed by the grave symptomatology of the primary affection (typhoid fever, etc.), to furnish a *point d'appui* for the diagnosis. Jaundice especially is absent, or, at least, is nowhere mentioned in the reports of this disease. The absence of icterus would not be remarkable in itself, did not Rokitansky expressly state that the finer bile-ducts are dilated, and the parts which are in a condition of croupous inflammation are occluded by inspissated bile in the shape of branching concretions. Perhaps croup of the biliary passages runs such a rapid course, or develops such a short time before death, that the increase of pressure, which is requisite for the passage of bile into the lymphatics, cannot develop within the bile-ducts. Perhaps, also, the secretion of bile ceases or is reduced to a minimum. The question as to the curability of croup of the bile-ducts, and to what further changes it may lead, can only be answered, as is evident from the previous remarks, by vague surmises.

Cases of pure idiopathic croup of the biliary passages, which are, therefore, not produced by the presence of foreign bodies or by an infectious disease, belong to the greatest rarities in the practice of medicine. Huenicken has reported a case of this kind which we will republish in abstract:

A man of mature age and vigorous constitution was taken sick, after dinner, with slight chilly sensations, insomnia, and loss of appetite. After the lapse of three weeks the physician, who had only been summoned at this period, noted a dark yellow, icteric color of the skin, a thick, white coating to the tongue, pain on pressure over the pit of the stomach, slight constipation. No appetite, no thirst, slight enlargement of the liver, no meteorism, spleen not enlarged. Pulse 80, regular, full. Urine of a dark brown, and, in addition to bile, contains some albumen; temperature not elevated. Sensorium somewhat dull. According to the statement of the patient, he suffers from dulness of comprehension; those around him have, for several days, noticed an increased tendency to sleep. The patient, who is very intellectual, gives incoherent answers which are understood with difficulty. The administration of infusion of senna produces copious evacu-

ations, which are partly brown, partly clay-colored; the condition of the patient is not changed thereby. After being questioned, he always relapses into a state of somnolence. As an inflammatory hepatic affection may, with great probability, be suspected, leeches were applied in the region of the liver, and infusion of senna with Glauber's salt, later calomel, were administered. The condition changed but little from the twenty-second to twenty-ninth days of the disease; one to three clay-colored, soft passages daily; restless nights alternated with quiet ones. Pulse continually 80. Pain on pressure in the region of the liver. Complete anorexia, but no feeling of thirst. The somnolent condition continues, the patient has visions in the day, is delirious at night, and, on questioning him, states that he sees everything yellow. The dark yellow color of the skin has gradually become bronzed; the urine is colored like ink. On the thirtieth day of the disease, the previously clay-colored stools again contained bile, and the urine was somewhat lighter. The return of bile in the stools had no influence upon the condition of the patient, the comatose state and the gastric symptoms, but the bronze color of the skin became somewhat brighter. On the thirty-sixth day the rapidity of the pulse increased to 110 beats, the stupor had increased, and the muscles of deglutition were paralyzed. Death occurred on the following day with the symptoms of paralysis of the brain. Autopsy about ten to twelve hours after death. About 300 grm. of brown fluid in the peritoneal cavity. The stomach empty, its mucous membrane covered with viscid mucus. Considerable dark yellow, viscid bile in the duodenum, mixed with intestinal mucus. The mouth of the ductus choledochus patent, large quantities of mucus containing bile in the small and large intestines, the intestinal mucous membrane hyperæmic, as in simple catarrh. The liver of normal size, the left lobe of usual consistence. The bile-ducts of this lobe allow a large quantity of brown, viscid bile to escape, certain larger ducts are coated with a dirty yellow, croupous exudation, which does not extend into the ductus hepaticus. The parenchyma of the right lobe, on the other hand, is more brittle, softer, and readily torn by the finger. Upon each cut surface, especially upon the upper edge, the various bile-ducts are found filled with purulent croupous exudation; in places, small abscesses enclosed in irregular walls have perforated the bile-ducts and communicate with the latter. The croupous exudation covering the bile-ducts could be removed from the walls like cream, without tearing, and in point of coherence was very like the croupous exudation which is generally observed in the large bronchi in the croup of children. The mucous membrane under the exudation is pale and not ulcerated; no bile is present in the ducts. Blood-vessels of the liver normal. Gall-bladder small, collapsed, contains no calculi. Its walls slightly thickened, the inner surface free from exudation, as are also the ductus cysticus and ductus choledochus. Spleen somewhat enlarged, kidneys pale and of a yellow color.

We have to deal in this case with an independent croupous inflammation of the bile-ducts, accompanied by inflammatory softening and abscess-formation of the liver tissue. From the

clinical history we may assume that the disease began as a simple catarrhal inflammation and then developed into croup, as the symptomatology of catarrhal icterus appears very plainly, and was followed, at a later period, by the signs of cholæmic poisoning.

Hemorrhage of the Biliary Passages.

Budd, Diseases of the Liver. German transl. by *Henoch*. Berlin, 1846. S. 187. —*Lebert*, Traité de l'anatomie patholog. 1861. T. II., p. 322 (Atlas, Pl. CXXVII.).—*Mettenheimer*, Beitrage zur Lehre von den Greisenkrankheiten. Leipzig, 1863. S. 101.—*Quinquaud*, Les affections du foie. 1 fasc. Paris, 1879 (Les hémorrhagies des voies biliaires, p. 1).

Although small extravasations may occasionally occur partly in the tissue of the mucous membrane, partly free in the lumen of the bile-ducts, especially in hyperæmic and inflammatory conditions of the latter, they do not, as a rule, make themselves noticeable and remain without significance. Extravasations into the biliary passages of any considerable extent, on the other hand, decidedly belong to the most rare occurrences.

The extravasated blood which is found in the interior of the biliary passages, is either derived from the walls of the latter or it has penetrated them from the exterior, and employs them as a channel of escape.

In some cases we must look for the cause of the hemorrhage in a congestion of the mucous membrane of the biliary passages; passive hyperæmia of the liver especially appears to lead to hemorrhages into the interior of the ducts. In a woman æt. fifty years, who was suffering from intense passive congestion of the liver in consequence of chronic disease of the heart, I found the gall-bladder filled with fluid blood, with scarcely any admixture of bile. The mucous membrane of the gall-bladder was markedly, though not diffusely reddened, but distinctly injected. Nothing abnormal was noticeable in the bile-ducts. The hemorrhage appears to have occurred per diapedesin in this case, as no rupture of vessels, bloody suffusion, or other lesion of this kind could be discovered. Mettenheimer's observation (l. c.) is of a

similar nature. This observer found hyperæmia of the liver in a woman æt. seventy-six years, who was suffering from chronic bronchitis, etc.; the contents of the gall-bladder consisted of cherry-red blood and two large tetrahedral gall-stones, and the mucous membrane was of a slate-gray color. In this case, also, the source of the hemorrhage could not be positively proven—whether it originated in the gall-bladder or was conveyed to the latter through the gall-ducts. The discharge of black, bloody masses from the mouth and anus, which had occurred in this patient, could be attributed to the round gastric ulcer which was also present.

Quinquaud (l. c. p. 18) reports a very remarkable case of hemorrhagic cholangoitis which, although the cause of its development could not be positively determined, extended over the entire system of bile-ducts, manifested itself by copious bloody stools, and led to death from the hemorrhage.

The patient, æt. thirty-one years, had had, as it appears, several attacks of hepatic colic. He had made a tolerable recovery from the last attack of this kind, which had occurred six months previously, when he was suddenly seized anew with pains in the region of the liver. On the third day of the disease very profuse bloody stools were passed by the jaundiced patient (the period when the jaundice began is not stated), and these were repeated once or several times daily during the disease, which lasted two weeks. On the eighth day the patient lost at one time a litre of blood in the stools; gall-stones were looked for in the evacuations, but were not found. The liver presented normal dimensions, the patient experienced acute pain upon pressure in the region of the gall-bladder. The pulse usually varied from 100 to 120 beats, the temperature from 38° to 39° (from 100.5° to 102.3°, F.). Rapidly progressing emaciation and extreme weakness, profuse viscid sweats, several syncopal attacks—in fact, the symptoms of acute anæmia form the chief features of the symptomatology, in addition to the greenish color of the skin and the profuse discharge of blood from the intestines.

Autopsy.—The markedly dilated stomach contains a black, "coffee-grounds" fluid, the duodenum is filled with coagulated blood and mucus. The diverticulum Vateri contains a firm plug of blood, which is lengthened toward the ductus choledochus and weighs 25 grm. The liver weighs 2,850 grm. The gall-bladder appears of considerable dimensions, is filled with clots of more or less changed blood weighing 135 grm. We may conclude from these data that the blood which escaped from the anus during life was derived from the bile-ducts and not from the intestinal canal. The hepatic and cystic ducts appear as markedly thickened firm cords; this is also true of the ductus choledochus, in which there is, moreover, no obstruction to the discharge, since the blood contained in the gall-bladder

flows freely into the intestines. The liver is extremely anæmic, and in general of a greenish to streaked-yellow appearance. Numerous blackish spots in the substance of the liver correspond to the lumina of the bile-ducts, which are filled with blood. The liver is interspersed with thick hard cords—the dilated, larger excretory ducts, which are filled with clots of blood. The blood appears to have remained in these canals for a long time; in some places it is blackish, or of a chocolate color, or like the lees of wine, in some coagulated or brittle, in others fluid or viscid. Upon pressure on the liver thick plugs of the decomposed blood project in all parts from the cut bile-ducts; but while these are distended with blood, the blood-vessels themselves appear entirely empty. If the hepatic bile-ducts are followed up by a pair of scissors, an abnormal connection of the former with the blood-vessels is nowhere visible. Even the smaller branches of the bile-ducts are so markedly dilated that the little finger can be introduced. The walls of the ducts within the liver are thickened from hyperplasia of connective tissue; in addition to the excessive vascularization, numerous and extensive ecchymoses are observed in them. On the other hand, no trace of an ulceration or of the formation of cicatrices can be found in the bile-ducts. In addition, the microscope shows the presence of numerous leucocytes in the thickened walls of the canals in question. All these data indicate an inflammatory condition, a cholangoitis, but concerning which it is doubtful whether it is primary or secondary. The intestine, finally, is filled with blood of a blackish red appearance. The quantity of blood is sufficiently large to explain the death of the patient. The walls of the intestinal canal show no pathological changes. The portal vein is empty, the hepatic artery normal.

The hemorrhages which occur into the bile-ducts during the course of certain constitutional diseases are also probably dependent on hyperæmia of the mucous membrane. Louis has several times observed in yellow fever the presence of fluid or coagulated blood, mixed with bile, in the bile-ducts, and Lebert found five times in seventy-two cases of grave icterus that the biliary passages were filled with blood.[1] Quinquaud (l. c.) reports, on the other hand, that in a man æt. forty-two years, who was suffering from marked hemorrhagic diathesis, the liver was found healthy, although in addition to numerous ecchymoses in other organs, the gall-bladder was found very markedly dilated by bile, and especially by soft clots of blood. In this case the alteration of the blood or of the walls of the vessels, *i.e.*, the hemorrhagic diathesis, appeared to be the only cause of the hemorrhage.

[1] Dictionnaire encyclop. des scienc. méd., par Dechambre, T. IX., p. 336.

Ulcers of the bile-ducts, especially the gall-bladder, also act, though exceptionally, as exciting causes of severe hemorrhages, attended by symptoms similar to those in hemorrhages from perforating gastric or duodenal ulcers. Budd (l. c.) gives the clinical history of a boy, æt. seventeen years, who had suffered from repeated hæmatemesis, and died of cholera soon afterward. The mucous membrane of the gall-bladder was found destroyed by numerous ulcers. There was nothing which indicated that the vomited blood could have been derived from any other source than the ulcerated gall-bladder.

Carcinoma of the bile-ducts can also be the starting-point for hemorrhage. The large biliary excretory ducts are then sometimes found filled with coagula of blood. Fauvel[1] describes a case of this character.

Finally, we must mention those hemorrhages whose origin is due to an accidental communication of a large blood-vessel with a bile-duct. To this category belongs the oft-quoted observation of Lebert (l. c.) in a woman æt. thirty years, of an aneurism of the hepatic artery which had ruptured into the gall-bladder, and had given rise to enormous hemorrhages into the stomach and intestines. In some cases, furthermore, a rupture of large hepatic blood-vessels, and, at the same time, of an adjacent gall-duct, has been found to follow contusions, a fall, etc., in which the blood escaped through the bile-ducts into the intestine, and gave rise to hæmatemesis and melæna. A similar abnormal communication between blood-vessels and bile-ducts within the liver may be produced by abscesses of this organ. Observations have been made, according to which, in such cases, not only did an extravasation of blood occur into the cavity of the abscess, but the blood flowed *en masse* through the eroded bile-duct into the intestine. Quinquaud (l. c.) quotes a case of this kind from Louis ("Recherches anatomo-pathol. sur diverses maladies," p. 367). This referred to a man, æt. twenty-two years, who, after a diarrhœa of long duration, suffered from repeated and very profuse hemorrhages from the intestinal canal, and died from the exhaustion caused thereby. At the autopsy, in addition to some

[1] Bull. de la soc. anat., 1838, p. 267.

smaller abscesses of the liver, another one was observed as large as a walnut, which was filled with a firm, black blood-clot. The bile-ducts, however, were found to be normal. Louis believes that the blood, in this case, which was discharged with the passages, was derived from the hepatic abscess. This assumption is not entirely credible, since, at the autopsy, a communication could not be found, either with neighboring large blood-vessels or with the bile-ducts, and, on the other hand, the cicatrices of six large ulcers were present in the neighborhood of the ileo-cæcal valves, together with numerous small ulcerations in the large intestine, so that the source of the bloody passages was, perhaps, to be looked for in the intestines. However, the entire course of the case renders Louis' view probable.

Nothing further can be said with regard to the clinical relations of hemorrhages of the bile-ducts, save that they generally remain latent, with the exception of rare cases, in which the hemorrhage is so great that the extravasated blood passes into the intestinal canal, and may reveal itself by hæmatemesis and bloody stools. With regard to the symptomatology of this condition we must refer to the above-mentioned case of Quinquaud and to Lebert's observation of an aneurismal sac which had ruptured into the gall-bladder, since there is no other material of this kind at our command. For this very reason it may appear premature to discuss the question as to the conditions under which we must look in the bile-ducts for the source of an internal hemorrhage, manifesting itself by hæmatemesis, and especially by bloody passages. Scarcely any explanation can be expected with regard to the character of the discharged blood, and the diagnosis of hemorrhages of the bile-ducts must therefore be based upon the fact that certain local symptoms are present on the part of the liver, while, from the circumstances of the case, hemorrhage of the stomach and intestines may be excluded. We must pay special attention to the presence of a tumor or hardness in the region of the gall-bladder, to pains in the region of the liver and gall-bladder (especially if there is a certain parallel between the hemorrhages and pains), to the circumference of the liver, jaundice, etc. Hemorrhage of the bile-ducts may be mistaken for

hepatic colic, in so far as the symptoms on the part of the liver come into question; the constitution of the stools would then prove decisive.

New-Growths and Tumors, especially Cancer of the Biliary Passages.

Durand-Fardel, Krankheiten d. Greisenalters. From the French by *Ullmann*. 1858, p. 928, and also in Arch. gén. June, 1840, and April, 1841.—*Icery*, Cancer des voies biliaires. Bull. de la soc. d'anat. 28 année. 1853, p. 73.—*Lambl*, Zottenkrebs des Gallenganges. Virch. Arch. VIII. 1855, S. 133.—*Markham*, Primary Cancer of the Gall-Bladder. Pathol. Trans. Vol. VIII., p. 243. 1857.—*Frerichs*, Klinik d. Leberkrankh. II., S. 454.—*Lebert*, Traité d'anat. pathol. T. II., p. 325.—*Foerster*, Handb. d. spec. pathol. Anat. 2. Aufl. 1863, S. 206.—*E. Wagner*, Prim. Krebs. d. Gallenblase. Arch. d. Heilk. 1863, S. 184.—*Rosenstein*, Icterus durch Cancroid d. Duct. choledoch. Berl. klin. Wochenschr. 1864. No. 34.—*Klebs*, Handb. d. pathol. Anat. I. 1869, S. 492 ff.—*Moxon*, Villous Cancer of the Gall-Bladder. Pathol. Trans., Vol. XVIII. 1867, S. 140.—*Villard*, Études sur le cancer primitif des voies biliaires. Mouvem. méd. 1870. No. 10-34, and Gaz. des hôp. 1872. No. 110.—Cf. Jahresber. v. Virchow und Hirsch for 1870. II., S. 174, and 1872, II., S. 171.—*Birch-Hirschfeld*, Lehrb. d. path. anat. 1877, S. 972.—*Jul. Schreiber*, Ueber das Vorkommen von primärer Carcinomen in den Gallenwegen. Berl. klin. Wochenschr. 1877. No. 31.—*Korczynski*, Prim. Carcinom. im Duct. hepat. Cf. Jahresber. v. Virchow u. Hirsch. 1878. II., S. 208.—*Moore*, Primary Cancer of the Gall-Bladder. Medical Times and Gaz. 1879, Dec. 20, p. 701.—*Copland*, ibid.—*S. Kohn*, Der primäre Krebs d. Gallenblase. Dissert. Breslau, 1879.

Albers, Atlas d. pathol. Anat. IV., Taf. 38, and Explanations, IV. 1. Abth. S. 490.—*Barrier*, Traité prat. des maladies de l'enfance. 3 éd. 1861. T. II., p. 218.—*Rilliet* and *Barthez*, Traité des maladies des enfants. 2 éd. T. III. 1861, p. 846.

The physician very rarely encounters new-growths and tumors in the region of the bile-ducts. Among these the cancer-like formations are by far the most frequent, and at the same time the most important in their consequences. In addition to the cancers and the extremely rare fibrous and myxomatous tumors, a few remarks should be previously made concerning the changes in the bile-ducts caused by tuberculosis.

Tubercular changes in the gall-bladder and large excretory ducts are unknown. A form of tuberculosis of the liver is very often observed, on the other hand, especially in children and young people, which manifests itself by so-called

tubercular cysts of the bile-ducts. The liver is infiltrated with numerous cavities from the size of a millet-seed to a pea, rarely also as large as a hazel-nut, which are filled with a bile-stained pap, and the walls of which consist of a cheesy infiltrated layer of varying thickness, averaging about 1–2 mm. The smallest foci of this kind appear as cheesy miliary nodules with a bile-stained and softened centre. In addition to these cavernous spaces the ordinary miliary tubercles of the liver also always appear in various stages of development.

The development of these biliary softening-cysts in tuberculous livers is not very readily understood, and has, therefore, led to various interpretations. According to one view these cavities are nothing more than cheesy conglomerates of hepatic tubercles, which have been saturated with the constituents of the bile after the development of necrosis, and have then degenerated into a brown pap. These conglomerates, therefore, stand in no close relations to the bile-ducts. According to another view, they are due to a tuberculous, cheesy infiltration of the walls of the finer bile-ducts, and to the ulcerative degeneration of the cheesy infiltrated walls, during which the bile is mixed into a pap with the detritus of the ulcers. The tuberculous affection of bile-ducts which is supposed to be present would form the analogue to cheesy peribronchitis and to the infiltrated tuberculosis of the mucous membrane of the genito-urinary tract. Arguments may be advanced in favor of both views, but it must be admitted that the anatomical connection of the cavernous spaces with the bile-ducts can only be exceptionally demonstrated with any amount of certainty. We must, therefore, still regard the question of the genesis of the so-called tuberculous cysts of the bile-ducts as an open one. Whatever answer may be found, the subject does not possess any practical significance since the change in question in the liver or its bile-ducts is in no wise revealed during life. It is always observed in the dead-house as an accidental and unimportant lesion.

Benign, non-carcinomatous tumors in the domain of the bile-ducts belong to the greatest of rarities. Polypoid growths on the mucous membrane of the gall-bladder and large excretory ducts are occasionally observed, but they do not merit any special attention on account of their very small dimensions. Albers (l. c.) refers to a case of submucous fibroid of the gall-bladder. This had a circumference as large as a five-groschen piece, was only two lines in thickness in the middle, and the mucous membrane of the gall-bladder above it was in a condition of ulceration. At another place, Albers also republishes a case which was described and depicted by Ehrmann, in which a fibroma as large as a bean was situated in the wall of the ductus choledochus. This had closed the canal and caused an enormous dilatation of the gall-bladder and all the bile-ducts, and very intense

jaundice. The mucous membrane of the gall-bladder was even torn in several places, and the external layers were distended like diverticula.

In the body of a woman, æt. fifty years, I recently found the gall-bladder considerably diminished in size, and its wall projecting forward in the shape of a large flat prominence. The organ appears as a hard, non-fluctuating tumor. Its walls are diffusely thickened, the cavity entirely filled by a papillary growth which adheres to the mucous membrane by a broad base and resolves itself into innumerable, partly short, club-shaped, partly narrow, long and branching papillæ of soft consistence and mucoid transparency. In places the papillæ appear opaque and of a milky white color. No trace of bile in the bladder, and only a small amount of tough mucus fills up the space between the papillæ. Microscopically the new-growth is shown to be a papillary myxoma with very regular short cylindrical epithelium at the surface of the papillæ, a great abundance of dilated coils of vessels, with fatty degeneration in many places, of the epithelium as well as the cells of the myxomatous tissue. This case appears worthy of mention, as it might readily have been interpreted as papillary carcinoma of the gall-bladder. With regard to the carcinomatous neoplasms of the biliary passages, we must, on account of the clinical aspects, make a sharp distinction between primary and secondary cancers of these organs. Primary carcinomata are, on the whole, of rare occurrence, while the secondary forms (metastatic and continuous cancers, more rarely metastatic sarcomata) are quite frequently observed in the gall-bladder as well as the large excretory ducts, in combination with carcinoma of the liver and other adjacent organs, or primary cancer at places farther removed. As a rule, the part taken by the biliary passages in the carcinomatous affection is so much inferior to that of the organ primarily involved, that it entirely escapes the attention of the physician, and is only made evident at the autopsy. Only those cases furnish an exception in which occlusion of the excretory ducts occurs with retention of bile, and marked and prolonged icterus, which constantly grows more intense ; the chapter on occlusion of the biliary passages should be consulted in this regard.

The secondary cancer appears, in accordance with the nature of the primary tumor, as scirrhus, encephaloid, colloid, or epithelial cancer. The metastatic (non-continuous) cancers appear usually in the form of nodules (either singly or in groups) which rarely exceed a moderate size (about that of a hen's egg), and may penetrate all the walls of the gall-bladder; they especially project toward the surface of the mucous membrane, and not infrequently pass into ulcerative or gangrenous degeneration. In addition, ulceration is sometimes observed in those parts of the mucous membrane which are not infiltrated with carcinoma. The degeneration of such cancers may give rise to perforation of the wall of the gall-bladder, and thus cause the passage of ichor and bile into the peritoneal cavity.

As a rule, continuous cancers of the gall-bladder, especially those which extend to the latter from the peritoneum (this occurs particularly in colloid cancer[1] of the latter) lead, on the other hand, to a diffuse superficial infiltration of the wall of the organ, and may finally extend over its entire surface. It can be distinctly seen with regard to infiltrated colloid cancers that they mainly follow the lymphatics of the subserous tissue, but spread thence into all layers of the gall-bladder until they reach the epithelium of the mucous membrane. The shape of the gall-bladder is not appreciably changed by the carcinomatous infiltration, but its walls become thickened to the size of the little finger and even larger, they become firm and rigid, while the cavity of the organ is correspondingly narrowed and its inner surface assumes an uneven, nodular character. Ulcerative degeneration also usually occurs in such a case; beginning in the mucous membrane it may spread over the entire inner surface and gradually involve the deeper layers, although perforation of the gall-bladder does not occur in these cases. The cavity of the organ is generally filled with an opaque, dirty gray ichor.

The conditions are very similar in secondary cancer of the large bile-ducts. This, indeed, frequently leads to occlusion of the affected ducts, but, on the other hand, the ulcerative degen-

[1] Cf. also *Luschka*, Gallertkrebs der Leber, Virch. Arch. IV. S. 400.

eration of the cancer often remains absent or only attains a very slight intensity.

A positive opinion with regard to the frequency of primary cancer of the biliary passages is obtained with difficulty. Only those cases manifest themselves undeniably as primary cancer in which the neoplasm is restricted to the biliary passages and all other organs are found free. When, on the other hand, carcinomatous neoplasms are observed in other places in addition to the biliary passages, some doubt may arise with regard to the original site of the disease, since neither the great extent of the cancer of the bile-ducts nor the signs of retrogressive metamorphosis evident in it, are a sure criterion that the cancer of the gall-bladder is really primary, although the other cancers which are present are of small size and fresh appearance. On the other hand, when, in addition to the bile-ducts, other parts, especially the liver and the organs in the vicinity, are found affected by the neoplasm, even a less extensive cancer of the gall-bladder, etc., may be primary, although the carcinomatous degeneration of the liver may have attained much greater dimensions and therefore appear as the chief seat of the affection. It is, therefore, advisable, in referring to primary cancer of the biliary passages, to take only those cases into consideration in which the organs mentioned are the sole site of the disease.

A considerable number of such cases have now been described. Primary cancer has been observed more frequently in the gall-bladder than the bile-ducts—both of the hard and soft, as well as alveolar and epithelial varieties. While primary cancers of the gall-bladder reach not inconsiderable dimensions, those of the bile-ducts usually do not exceed a very moderate size, perhaps that of a cherry.

Cancer of the gall-bladder usually forms a flattened or nodular infiltration of the wall about the thickness of a finger, which involves a large portion of the organ or extends over its entirety. In the latter event the cancer may appear as a hard tumor as large as a fist. As a rule the cavity of the gall-bladder is so much more narrowed, the larger the portion of the wall which has been affected by the cancer. Especially noteworthy is the fact that, in the majority of cases, the organ, which is in a con-

dition of cancerous degeneration, is not filled with bile, but with a gray pap (the detritus of the cancer which has partly undergone ulcerative degeneration), and, in addition, with gall-stones of varying number, size, and constitution. The hard, thickened wall of the organ has several times been found stretched taut upon the immovable, imbedded gall-stones; the latter lay in ditch-shaped excavations and appeared to be pressed into the cancerous mass. The inner surface of the organ is usually covered very irregularly with warty or papilliform cancerous proliferations, which are subject to ulceration at an early period. The cystic duct is often found closed, especially when the cancer of the gall-bladder extends to this canal.

Primary cancers of the biliary passages may develop at any part of the large excretory ducts, either within or without the liver, but they are preferably situated, as it appears, at the intestinal end of the ductus choledochus and at the bifurcation of the hepatic duct. Under certain circumstances some attention is requisite to discover them, on account of their small size and concealed position. They usually form a ring-shaped infiltration of the wall of the affected canal, which is attended with considerable narrowing or complete closure of the lumen of the duct. In this event, also, the inner surface of the cancerous ring is sometimes smooth, sometimes superficially ulcerated, at times covered with papillary or warty growths.

To the examples of cancer of the bile-ducts, which have been collected by Villard and Schreiber (l. c.), I add a case under my own observation, which may serve as a type of the anatomical relations of primary cancer of these organs:

A man about sixty years old, who had suffered for months from intense jaundice, finally died of exhaustion after rapidly increasing emaciation. The liver was enlarged, firm, slightly granular, of an olive-green color, all the bile-ducts within the liver were diffusely dilated and filled with pus slightly tinged with bile. The hepatic duct was affected at its bifurcation for a distance of two ctm. by a firm, scirrhous growth. The lumen of the duct appeared, on cross-section, as a narrow fissure of an irregular angular shape, which was with difficulty traversed by a sound. The wall of the duct is converted by the cancerous infiltration, which involves its entire circumference uniformly, into a rigid mass of tissue about three mm. in thickness, upon section of which the separate layers of

the wall can no longer be distinguished. The cancer extends downward to the connective-tissue sheath of the duct and appears here to be quite sharply defined. The inner surface of the canal in the region of the cancer is irregular, nodular, and covered with flat, warty excrescences, but even the beginning of the formation of ulcers is nowhere visible. In other respects the bile-ducts presented a normal appearance. No cancer could be discovered either in the neighborhood of the cancer of the bile-duct or in any other part of the body. The microscopical examination in this case left no doubt that the cancer started in the epithelium of the glands of the bile-ducts. In most places the cancer-cells were, even in the deeper layers, involved in a myxomatous metamorphosis, and many alveoli only contained vitreous, mucoid masses in addition to some degenerated cells. The neoplasm may therefore be termed colloid cancer of the bile-duct.

As far as regards the development of primary cancer of the biliary passages, we very frequently meet with the assertion, especially in French writers, that the new-growth takes its origin in the submucous tissue. This is true if it merely indicates the region in which the cancerous proliferation of the cells commences, but it is most probably incorrect if we regard the submucous cellular tissue as the "mother tissue" of the cancer. My own observations indicate, with regard to cancer of the bile-ducts, that the epithelium of the glands of the ducts is the starting-point for the cancerous cell-proliferation. Birch-Hirschfeld has arrived at the same opinion with regard to cases of primary cancer of the bile-ducts examined by him. Klebs contends, with regard to primary cancer of the gall-bladder, that it starts from the epithelium of the organ and its (poorly developed) mucous glands.

Etiology.

The first six cases of primary cancer of the biliary passages, which were published by Durand-Fardel, were obtained from the material of the Salpêtrière, a woman's hospital. Perhaps the statement of some authors, that this form of cancer has been observed much more frequently in the female sex, is attributable to this circumstance. Other authors maintain, on the contrary, that there is a marked preponderance of the male sex in this direction. The more, however, that observations of primary cancer of the biliary passages are collected, the more it appears to

be proven that the disease occurs with almost equal frequency in both sexes.

But if, in fact, it should be shown, that especially the primary cancer of the gall-bladder develops much more frequently in women, we might surmise that this circumstance stands, perhaps, in causal connection with the demonstrably greater frequency of gall-stones in the female sex. It has been previously mentioned that, in primary cancer of the gall-bladder, the cavity is very often found filled with concretions—too often to allow this coincidence to be regarded as the result of chance. The simultaneous appearance of cancer in the wall of the gall-bladder and of gall-stones, has been variously interpreted. Some explain the formation of calculi as a result of the stasis and decomposition of the bile in the gall-bladder, which has been hastened by the cancer. Others believe, on the contrary, that the continued presence of the gall-stones within the organ, and the mechanical irritation which the calculi exert upon the walls, should be regarded as the exciting cause of the carcinomatous new-formation, inasmuch as they rely upon our experience that cancers often develop in other places which are subject to a continuous slight mechanical irritation. Arguments may be adduced for and against these views, but the controversy cannot be decided at present. For our own part we incline to the opinion of those who regard the gall-stones as the exciting cause of the carcinomatous new-formation in predisposed individuals.

Primary cancer of the biliary passages is especially observed in those individuals who have already passed the fiftieth year of life. Durand-Fardel's observations were even made upon five women at the age of seventy-one to seventy-five, and one of eighty-one years. But such cancers also appear earlier, between the fortieth and fiftieth years. Markham's (l. c.) case, which referred to a woman æt. twenty-eight years (the gall-bladder was found filled with stones), may be regarded as a rare exception. Heredity appears to play no part among the causes of these cancers (Villard).

Symptoms. Diagnosis.

All observers are agreed that cancers of the biliary passages, as a rule, produce no very characteristic symptoms; that the diagnosis is therefore usually uncertain, and that it is very difficult to avoid mistaking these growths for certain other diseased conditions, especially for cancer of the pylorus and duodenum.

In cancer of the gall-bladder pain is almost always present in the region of the organ, whence it radiates over the right hypochondrium (fifteen times in seventeen cases of Villard). The pains are usually dull, heavy, continuous, at times they become very acute, and assume a lancinating character. At times the pains appear similar to those of hepatic colic, which may probably be explained by the usually coincident presence of gall-stones in the gall-bladder. Solitary cancer of the bile-ducts, on the other hand, produces no noteworthy pains, at least I find no mention made in the histories of the cases in question, and often, indeed, the absence of pain is expressly mentioned.

A tumor in the right hypochondrium, probably due, in great part, to the thick-walled gall-bladder, and of hard, immovable consistence is mentioned by Villard eleven times in seventeen cases. The tumor may attain the size of a child's head; it is egg or globe-shaped, and at times feels nodular. Although the presence of a tumor is mentioned by the majority of observers, it could not always be referred to the gall-bladder, but was often erroneously attributed to the duodenum or pylorus. A tumor cannot be discovered in cancer of the gall-ducts on account of its small size and concealed position.

Icterus, with all its sequences, is not necessarily present in cancer of the biliary passages, though it frequently occurs. Villard found well-marked jaundice fourteen times in seventeen cases. Since it is dependent on occlusion of the gall-bladder, it cannot be looked for in solitary cancers of this organ, but only (then, however, always) when, in addition to this, cancer of the excretory ducts is also present, as is so frequently the case. When icterus has once appeared it continues to increase, as a rule, and may rapidly attain the highest intensity, and especially go hand-in-hand with complete discoloration of the fæces.

Digestive disorders of various kinds, especially anorexia, fulness and pressure in the region of the stomach, constipated bowels, etc., which may be attributed, in part, to the coexisting icterus, almost always occur in cancer of the biliary passages, but present nothing characteristic, and can, therefore, be scarcely relied upon for diagnostic purposes. When cancer of the gall-bladder produces pressure upon the duodenum, emesis may develop, as occurred in Markham's case, which presented all the symptoms of cancer of the pylorus. Bloody stools and hæmatemesis are mentioned by several observers.

Occlusion of the bile-ducts from cancer is sometimes followed, in addition to dilatation of these canals, by purulent catarrh of the latter. Intermittent exacerbations of fever may then occur, such as also develop in occlusion of the canals from other causes. Villard mentions these febrile attacks three times among his seventeen cases.

Finally, we must mention the cancerous cachexia—the rapidly increasing emaciation and weakness of the patient, the sallow complexion (when icterus is absent)—as an integral symptom in cancer of the biliary passages.

The diagnosis is always difficult, and especially in cancer of the bile-ducts, almost impossible. Cancer of the gall-bladder is indicated, above all, by the hard, slowly growing, and painful tumor in the right hypochondrium. If the symptoms of cancerous cachexia appear, and marked improvement of the patient occurs at no time, the assumption of a cancer of the gall-bladder is justified. Mistakes are possible in so far as the starting-point of the tumor is not always attributed to the gall-bladder, but to the pylorus, duodenum, or transverse colon, an opinion toward which we will be more inclined when the remaining symptoms of the patient indicate a chronic disorder of the stomach and intestines.

Cancers of the bile-ducts reveal themselves neither by the appearance of a tumor nor by pains; they rather produce a rapidly increasing, uninterruptedly progressing jaundice, which continues with equal intensity until death, with all the other symptoms of stasis of the bile, enlargement of the liver, etc. That the occlusion of the bile-ducts is due to cancer in a concrete

case may be surmised with a certain degree of probability, though never surely proven, from a consideration of the age of the patient and his condition of nutrition (cachexia).

Duration, Terminations, Prognosis.

The duration of the morbid symptoms in cancer of the biliary passages is usually placed at four to six months or more, in individual cases at several years. The disease assumes an insidious but constant, uninterrupted course, and, under any circumstances, terminates in death. The duration of the disease appears to be shortened by the development of icterus. The prognosis is unfavorable in every particular.

Treatment.

There can be no question of treatment of the primary disease. As the suspicion is warranted that the presence of calculi in the gall-bladder may prove the exciting cause for the development of cancer of this organ, the physician again finds himself called upon to devote careful attention to the prevention and removal of cholelithiasis. In other respects the treatment must be purely symptomatic. It must be directed against the pains which appear in the region of the gall-bladder (in which hypodermic injections of morphine will, perhaps, prove of greatest service), furthermore, against the symptoms connected with jaundice, especially the pruritus, the tendency to constipation, the digestive disturbances, and, finally, attention should be paid, as far as possible, toward counteracting, by a suitable diet, the rapid deterioration of general nutrition.

Disorders in the Canalization of the Biliary Passages.

Introductory Remarks.

Canalicular disorders—in the broadest sense—assume a prominent position among the pathological conditions of the biliary apparatus. It would, perhaps, be difficult to mention a disease

of the biliary passages in which the factor of canalicular disturbances must not be taken into consideration. In many diseased conditions of these organs this disturbance constitutes the main feature of the entire affection, and is responsible for the general character of the symptomatology.

In all cases of marked disturbance of canalization we find that the lumen of the excretory bile-duct is narrowed or entirely occluded in one spot, while at the same time other portions of the canal appear dilated. The connection between these abnormal conditions consists in the fact that stenosis develops at some part of the excretory duct, and that the difficult escape of bile resulting therefrom causes stasis of bile behind this spot, and therefore leads to a corresponding dilatation in those portions of the canals which are situated in its region of supply. The stenosis of the canal will, therefore, in every case, constitute the primary factor, and dilatation of the other bile-ducts, the secondary one in the general canalicular disturbance. It therefore follows that, in the consideration of the latter, we must start with the stenosis and occlusion of the biliary passages.

The next most important point concerns the locality at which the stenosis develops, since upon this depends what parts of the system of bile-ducts will be effected by the secondary changes of biliary stasis and dilatation. Most disastrous are the effects of occlusion of the common excretory bile-duct. The biliary stasis then extends over the entire system of bile-ducts ; the gall-bladder and ductus cysticus, together with the hepatic duct and all its coarse and fine ramifications, experience from the retained secretion a dilatation which is often enormous. Occlusion of the ductus hepaticus, or its two chief hepatic branches, is not much more favorable, as the biliary stasis and dilatation then involves all the bile-ducts situated within the liver, while the gall-bladder and ductus cysticus and choledochus are empty, and do not functionate. If only one or another principal bile-duct in the liver is occluded, the changes mentioned will remain confined to the hepatic lobe which is implicated, while the closure of some of the smaller ducts within the liver will produce changes which are correspondingly circumscribed, and often present no appreciable consequences.

When the stenosis affects the cystic duct, its results are entirely different. The system of bile-ducts remains entirely unaffected by these changes, and the latter are confined exclusively to the gall-bladder, which is now thrown out of communication with the other biliary passages, and can neither receive bile nor discharge the contents which it may happen to have. Under such conditions, either atrophy and obliteration of the gall-bladder develops, or, on the other hand, an abnormal dilatation of the organ with the appearance of hydrops vesicæ felleæ, or dropsy of the gall-bladder.

The radical differences in symptomatology which result from the location of the stenosis or occlusion of the ducts, make it appear proper to discuss the entire subject of canalicular disorders in two separate chapters, one of which will be devoted to closure of the ductus choledochus and hepaticus, or the stasis and retention of bile, and the other to dilatation of the gall-bladder.

Stenosis and Occlusion of the Biliary Excretory Ducts.

(Ductus choledochus and Ductus hepaticus.)

Stasis and Retention of Bile.

Andral, Clinique médicale, 4 éd. T. II., p. 520. Paris, 1839.—*Bright*, Observations on Abdominal Tumors, Guy's Hospital Rep. V., p. 298. 1840.—*Ibid.*, Cases and Observations connected with Diseases of the Pancreas and Duodenum. Med.-Chirurg. Trans., Vol. XVIII., p. 1 (1833).—*Schaefer*, De hydrops ductuum biliarium. Diss. aug. Turici, 1842.—*Budd*, Diseases of the Liver. German by *Henoch*. 1846, S. 198 ff.—*Henoch*, Klinik d. Unterleibskrankheiten. I., S. 93 ff. 1855.—*Frerichs*, Klinik d. Leberkrankhten. I., S. 138. 1858, etc.—*West*, Diseases of Infancy and Childhood. 4 ed. 1859. p. 570.—*Bristowe*, Trans. of the Path. Soc., Vol. IX., p. 225.—*Binz*, Congenitale Obstruction d. Gallenwege. Virch. Arch. XXXV., S. 360.—*Wyss*, Zur Aetiologie des Stauungs Icterus. Virch. Arch. XXXVI., S. 454.—*C. E. E. Hoffmann*, Verschluss der Gallenwege durch Verdickung der Wandungen. Virch. Arch. XXXIX., S. 206.—*Hoffmann, ibid.*, XLII., S. 218.—*Fritz*, Ueber narbige Stenosen des Ductus choledochus. Diss. aug. Berlin, 1868.—*Baehr*, Die Ursache der Verengerung beziehtl. Verschliessung d. Gallenausfuehrungsgaenge u. ihre Diagnose. Diss. Berlin, 1870.—*Hirschsprung*,

Angeborener Verschluss der Gallenausfuehrungsgaenge, Hosp. Tidende, 2 R. IV., 35, 1877 (Compilation of twelve similar cases in abstract, in Schmidt's Jahrb. Bd. 177, S. 31. 1878, No. 1).—*Strauss*, Des ictères chroniques. Paris, 1878.—*Donop*, De ictero speciatim nervatorum. Diss. inaug. Berlin, 1828.

Every stenosis of the biliary excretory ducts is equivalent to interference with the discharge of bile into the intestines. As soon as it reaches a certain grade, absorption of the retained bile occurs and jaundice develops, viz., true stasis or absorption icterus. It is not our province, however, to discuss all the details of absorption icterus and all the anatomical changes of the bile-ducts to which it is due. We will rather confine ourselves chiefly to those cases in which the obstruction to the flow of bile is complete and, at the same time, permanent, and in which, therefore, chronic, even fatal, jaundice occurs. We exclude from consideration, on the other hand, those cases of temporary stenosis, for instance, the category of so-called catarrhal icterus, and furthermore, the temporary jaundice connected with the passage of gall-stones and parasites through the biliary canals, or produced by the pressure of the pregnant uterus or the large intestines, when filled with fæces, upon the excretory ducts of the bile. *A priori*, a sharp differentiation of the subject under consideration cannot be carried out, nor is it even necessary. How far this is possible will be determined in the section on etiology.

Etiology.

The manifold character of the causes which may give rise to closure of the biliary excretory ducts, makes it desirable to take a general survey of the subject. We may take as the starting-point in this particular either the situation or the pathological character of the etiological factors. The causes of the occlusion are either situated, 1, in the lumen of the duct, which, although normal in other respects, is filled and distended by some object; or 2, in the wall of the duct, inasmuch as this is so changed by certain pathological processes that the canal is impermeable to the bile at the position in question; or finally, 3, outside of the canal in such a manner that the duct, although unchanged itself, becomes impenetrable. Certain causes, indeed, act in several,

and perhaps in all three ways, even in a given case, so that, for instance, a carcinomatous neoplasm may compress the excretory duct, infiltrate its walls, and finally grow into the lumen.

With regard to their nature the causes may again be chiefly collected into three groups which may be differentiated as, 1, *foreign bodies*, which lie in the lumen of the canal and fill it; 2, *inflammatory processes* with new formation of cicatricial connective-tissue masses, which are followed at times by an organic closure of the canal from adhesion of its walls, at times give rise to a sort of cicatricial stenosis of the duct (without entire disappearance of its lumen), or may also lead, from without, to occlusion of the canal by simple compression; 3, *neoplasms and tumors* which present the greatest variations with regard to character, situation, mode of development, etc., and may give rise to impermeability of the excretory duct by compression as well as obstruction of the lumen or in any other way. The following points must be emphasized in the special cases:

1. *Occlusion of the biliary excretory ducts by bodies which obstruct their lumen.*

This refers, in the first place, to gall-stones which, during their passage from their place of development (the gall-bladder, or, much more rarely, the hepatic ducts) toward the duodenum, have remained in the common gall-duct and, as we usually say, have become impacted. The narrowest parts of the canal through which the gall-stones must pass, are the ductus cysticus, especially at the place at which it bends near the neck of the gall-bladder, and the duodenal end of the ductus choledochus, the narrowest part of which corresponds to its opening, the porus biliarius. The wall of the duct closes firmly upon the surface of the calculus, is stretched taut over the latter and, unless the stone has a very peculiar conformation, the bile will be unable to flow alongside. As a rule, however, the impaction of gall-stones in the intestinal end of the ductus choledochus only lasts a short time, after which they are expelled. Permanent retention of the calculi in the ductus choledochus only occurs in rare cases,[1] for the reason that stones which are unable to pass through

[1] *Vide*, among numerous other cases, that of *Graubner*, Arch. d. Heilk. VI., 1865, S. 184.

the duct on account of their size, will usually remain impacted in the duct of the gall-bladder. The gall-stones, which are retained in the duodenal end of the ductus choledochus, generally give rise to a circumscribed inflammation of the canal, during the course of which a sort of encapsulation of the stone occurs, so that, at a later period, the excoriated inner surface of the duct appears as if adherent to its surface. Later, however, when ulceration of the wall occurs, the concretion, which has been hitherto firmly enclosed in the walls of the canal, may become loosened. If, in such a case, the calculus itself should not advance and be pushed into the intestine, the loosening may, however, have the good effect that the flow of bile, which had previously been entirely stopped, again begins, even though to a very limited extent. In those cases in which gall-stones have formed in the large hepatic bile-ducts, their spatial relations to the lumen of the canal will only, in rare cases, be so unfavorable that the flow of bile is thereby entirely interrupted. As a general thing, the bile will effect a passage between the calculi and the walls of the duct, and the consequences of the stenosis will be less evident than in complete occlusion of the ductus choledochus.[1]

In the second place we must consider certain parasites[2] which occasionally fill the lumen of the large biliary excretory ducts. Among these the echinococcus takes the first rank. We do not refer to those cases in which a hydatid tumor of the liver causes jaundice from compression of individual hepatic ducts, but rather to the case in which a ruptured echinococcus sac opens toward the bile-ducts and partially allows its contents to empty into the latter. The occlusion of the bile-ducts produced in this manner by echinococcus vesicles is, however, usually temporary, as the gall-ducts generally empty their contents into the intestines under symptoms similar to those of hepatic colic. At times the bile-ducts become sufficiently dilated to permit a complete discharge of the echinococcus sac into the intestine. But this rarely occurs, as the majority soon run a fatal course in this or that manner. I am unacquainted with any example in which closure

[1] *Vide* the further remarks in the later section on cholelithiasis.

[2] Parasites of the biliary passages will be discussed at a later period in a special chapter.

of the ductus choledochus by means of worms of the gall-bladder has finally caused the death of the patient solely as the result of the chronic retention of bile produced thereby. Charcot's case,[1] in which complete occlusion of the ductus choledochus occurred from echinococci, is worthy of note; the cyst, from which they were derived, was found empty, but had been torn in consequence of the stasis of bile, so that fatal peritonitis developed.

Matters run a different course in multilocular echinococcus tumors of the liver. Experience teaches that this condition leads, in the majority of cases, to closure of the biliary excretory ducts and to chronic jaundice lasting until death. The ductus choledochus is rarely reached by the multilocular echinococcus, but it spreads sooner or later to the hepatic duct and its two chief branches, often also to the cystic duct, and even to the wall of the gall-bladder. At first a sort of infiltration of the walls of these canals and their immediate neighborhood occurs, sometimes over their entire circumference, sometimes only on that portion which is turned toward the liver. The walls of the ducts then become rigid, their lumen narrow, finally the small vesicles of the worms penetrate *en masse* into the cavity of the ducts and fill them over a greater or less area. In the further course of the disease the ulceration of the infiltrated portions may begin in the interior of the bile-ducts. In several unpublished cases I found the gall-bladder, cystic duct, and the two branches of the hepatic duct together with the trunk of the latter ulcerated, while the principal tumor in the liver was still intact or the softening-cavity present in it had formed independently of the ulceration in the territory of the large bile-ducts. It is unnecessary to dilate upon the fact that the ulcerative degeneration of those portions of the bile-ducts which are infiltrated with echinococci cannot have the effect of restoring the flow of bile.

Stenosis of the bile-ducts and an obstruction to the escape of bile may be caused by the presence of liver flukes and round worms. However, the jaundice which is usually, though not by any means without exception, found in these cases, cannot be exclusively attributed to the occlusion of the lumen of the canal by the body of the worm. The inflammatory changes, which

[1] Compt. rend. de la Société biolog. 1854. 2 sér. T. I., p. 99.

develop in various grades of intensity in the bile-ducts as well as in the tissue of the liver on account of the presence of the parasites, are at least equal in importance to the first factor, as will be shown in the description of this diseased process which will follow.

Foreign bodies, other than those mentioned, very rarely occur in the biliary excretory ducts. It is rendered almost impossible for foreign bodies to pass from the duodenum into the ductus choledochus on account of the narrowness of the opening. In those very exceptional cases in which a cherry-pit, the seed of a gooseberry, etc., have made their way into the common duct and given rise to jaundice, the opening of this canal has probably been considerably dilated previously from the passage of gall-stones. Nor has closure of the biliary excretory ducts by firm coagula of blood been hitherto observed as the cause of permanent retention of bile.

2. *Stenosis and occlusion of the biliary excretory ducts by inflammatory processes with new-formation of cicatricial connective tissue.*

The cases belonging to this category must be regarded as typical representatives of the conditions of permanent retention of bile, which finally run a fatal course without the addition of other causal or complicating factors. But here also various modifications in the condition of the excretory ducts must be mentioned, since either complete obliteration of the lumen of the canal may occur, or the lumen is retained, but the canal remains, at the same time, entirely impermeable. It appears judicious to differentiate the following conditions, which vary partly pathogenetically, partly anatomically.

a. The lumen of the ductus choledochus has disappeared in some part of its course without leaving a trace, there is true atresia or imperforation of the canal,[1] inasmuch as the inner surfaces of its walls which are in apposition, have come in contact and organically united. The occlusion may extend over a variable length and occur at any point in the course of the canal.

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[1] We now refer only to acquired occlusion. *Vide* below for remarks on congenital occlusion of the ductus choledochus.

It is usually situated in the region of the pars intestinalis of the duct; occasionally it only affects its extreme end, the porus biliarius. The intestinal end of the pancreatic duct is also closed at times on account of one and the same process. In the region of the obliteration is found a compact mass of fibrous tissue, at times very similar to a cicatrix, at which, upon autopsy, usually no trace of the wall of the original canal is discoverable.

With regard to the causes and pathogenesis of the acquired obliteration of the ductus choledochus in middle and advanced age, we must regard it as a necessary premise that, in the region of the later obliteration, a part had existed devoid of epithelium, excoriated, and covered with granulations, since the obliteration is produced by the organic adhesion, *i.e.*, union of two granulating surfaces in immediate contact with one another. The question only remains to be discussed as to the cause of the fact that a portion of the inner surface of the canal becomes excoriated, ulcerated, and, at a later period, covered with granulations. In this respect we must rely upon surmises. Ulcers in the ductus choledochus may be caused by gall-stones, especially when the latter, during their progress toward the intestine, have been retained for a long period in a certain portion of the canal. These ulcers form more rarely during the course of severe typhoid fevers and other severe infectious diseases, that is, without the aid of any coarse mechanical influences. I believe, however, that simple excoriations upon the inner surface of the ductus choledochus (without more deep-seated ulceration) may suffice to lead to obliteration of the duct. Such excoriations may develop in any severe catarrh of the canal, and, therefore, also in simple catarrhal icterus, however this may have been produced. I would regard a simple catarrh of the canal as the starting-point of the later obliteration in those cases in which there has been no history of gall-stone colic, typhoid fever, or similar conditions, in which, however, the jaundice (which has since become chronic) had, from the coexisting conditions (symptoms of gastric and intestinal catarrh), been regarded as simple icterus, and an early recovery might have been predicated. Since catarrhal icterus is a very frequent disease which may develop under the most variable external conditions of life in individuals of all ages, and

from the most manifold causes, we may fall back upon that mode of development of obliteration of the ductus choledochus just described, in all cases in which a more plausible explanation cannot be given, and where the concomitant symptoms at the beginning of the jaundice are similar to those of catarrhal icterus.

In this category belongs also the rare case in which the mouth of the ductus choledochus is closed by cicatrization of a perforating duodenal ulcer, which has extended into the region of the porus biliarius. The effects are, of course, similar to those in obliterations in the course of the ductus choledochus. An instructive case of this kind is found in Murchison.[1]

b. True stenosis or cicatricial stricture of the excretory duct, which is due to fibroid thickening and rigidity of the wall of the canal or of the connective tissue immediately surrounding—a complete analogue of urethral strictures—is characterized by the fact that the lumen has not entirely disappeared at the place of stricture, although it may be narrowed down to entire impermeability. Upon transverse section of the stricture the lumen appears as a narrow fissure surrounded by firm walls, or as a punctate opening, which allows the passage of a fine sound, even when there was complete retention of bile during life. These strictures occur not only in the ductus choledochus, but also, and probably with equal frequency, in the ductus hepaticus, especially at its bifurcation into its two chief branches, or only in the right or left[2] hepatic duct. The length of the stricture varies from a few millimetres to about 3 or 4 ctm. and more.

With regard to the origin of these strictures,[3] they cannot, by any means, be all interpreted as cicatricial strictures in the narrower sense. Certain strictures develop undoubtedly in the following manner, viz.: An ulcer, which had been previously present in the bile-ducts, has cicatrized, and the retracting cicatrix has narrowed the lumen of the canal. We can determine the presence of the cicatrix of an ulcer by the fact that the mucous membrane of the duct in the affected portion no longer presents its original appearance which is so well characterized by

[1] Lectures on Diseases of the Liver. 2 ed., p. 376 (Case 122).

[2] As in the case described by *Bristowe*, Trans. of the Path. Soc., Vol. IX., p. 223.

[3] Cf. *C. E. E. Hoffmann's* remarks in Virch. Arch. 39 Bd. S. 206.

the hollow recesses, situated at regular intervals and corresponding to the orifices of the glands of the bile-ducts. As probably the majority of this variety of ulcers are due to gall-stones, which have passed through the ductus choledochus, the true cicatricial strictures are situated by preference in the course of this canal. Cases occur, however, in which the biliary excretory duct is inclosed in nodulated fibrous tissue, and, being indissolubly united with it, appears to have undergone complete stenosis, although no deviation from its original appearance can be observed upon the inner surface of the duct. These connective-tissue hyperplasiæ, which are sometimes diffuse, sometimes quite sharply defined, appear to be the product of a chronic phlegmonous inflammation, which almost always runs a latent course, and is confined to the wall of the duct and its immediate vicinity. The causes which give rise to these phlegmonous processes are usually no less latent. The possibility that catarrhal inflammations within the bile-ducts may spread to the entire thickness of their walls and here continue in the form of a chronic phlegmon, while the catarrh, in the narrow sense, has perhaps already disappeared, is undoubtedly worthy of being taken into consideration, and also that inflammatory processes which have developed in the vicinity (we are at once reminded of chronic peritonitis, especially perihepatitis, etc.) may be propagated [1] to Glisson's capsule and to the walls of the bile-duct.

In the Tübingen Medical Clinic a shepherd, æt. forty years, was treated who was taken sick in the beginning of March, 1876, with headache, a tired feeling, anorexia, frequent eructations without vomiting, and constipation. Jaundice was soon superadded, rapidly attained a high grade, and continued uninterruptedly ever since until death, which occurred after the disease had lasted a year. The passages were entirely destitute of color from the beginning of April, and continued so since that time. Attacks of pain and fever were absent during the entire course of the affection. No cause for the disease could be discovered; gross errors of diet, alcoholism and syphilis could be excluded. Death occurred in the beginning of March, 1877, after progressive emaciation, œdema of the lower limbs, and marked cholæmic symptoms. A pleuritic exudation on the left side had developed four weeks previously. The autopsy showed: a dark icteric

[1] *Vide* among other cases, that reported by *Hoffmann* (Virch. Arch. 39 Bd. S. 200), who also republishes a similar one by *Mehrbach* from Kuechenmeister's Ztschr. f. Med., etc. N. F. II. 1863, S. 363.

color, as well as numerous ecchymoses in the skin, etc., about three litres of brownish serum in the peritoneal cavity, and at least as much in the left pleural cavity. A certain amount of rigidity, together with a slight, uniformly distributed opacity can be recognized in the peritoneum, and are the results of a mild chronic peritonitis. The liver about normal in size, no bile in the gall-bladder, which is filled, like the cystic duct, with colorless mucus. The ductus choledochus entirely normal, its mucous membrane unstained. The hepatic duct, on the other hand, is compressed along its whole length as far as its bifurcation into both hepatic branches by nodular masses of connective tissue, which is about four mm. in thickness, firmly united to the wall of the duct and encircles the latter like a ring.

The wall of the canal is distinguishable by the eye from the fibrous mass and surrounding tissues, its lumen is changed into a rigid narrow fissure from 3 to 4 mm. in breadth, and with difficulty permits the passage of a fine sound. At the point of stricture the mucous membrane of the duct shows the normal, ridged appearance, is not stained with bile, and is free from cicatrices, ulcers, and other changes of this character.

All the bile-ducts within the liver are enormously distended to a full finger's-breadth, and filled with a clear, mucoid, pale-green fluid. The parenchyma of the liver is of a dark olive green, firm, anæmic, and the interlobular connective tissue is considerably increased. The portal vein has only united with the fibrous mass on one side in front of the porta hepatis; otherwise it is free, and therefore not really compressed. The spleen is about five times larger than normal, and very soft.

c. The inflammatory new-formation of connective tissue, which forms the starting-point for impermeability of the biliary excretory duct, may also develop from the peritoneum and the subserous tissue on the inferior surface of the liver; it may, therefore, be the result of perihepatitis.[1] Such inflammatory thickenings of the peritoneum, which develops as firm ridges and cords in the region of the transverse fissure, will in themselves, but even more by their innate tendency to retraction and shortening, exercise serious pressure upon the bile-ducts and narrow their lumina to a marked extent, or even entirely obliterate them. The perihepatitis sometimes occurs over a very circumscribed area, sometimes over a greater surface; it may exist alone or form part of a general peritonitis. Among the common causes of this perihepatitis we must mention certain diseases of the liver (cirrhosis, etc.), general peritonitis, inflammations of the right pleura,

[1] Cf. the case in *Frerichs*, Klin. d. Leberkr., I., S. 159.

perforating ulcer of the stomach, and, above all, constitutional syphilis.

3. Finally, we must also refer under this category to congenital occlusion of the biliary excretory duct, as an examination of the cases in question compels us to assume that we do not have to deal with an original vice of formation, but that the bile-duct was primarily normal and permeable, and only became occluded at a later period. The occlusion itself sometimes occurs at a later, sometimes at an earlier period of intrauterine existence. In the first event we find, instead of the permeable ductus choledochus, only a solid, fibrous cord; in the second case, hardly a trace is even left of such a structure. The occlusion and obliteration may simultaneously involve the cystic duct and the gall-bladder, while the bile-ducts within the liver are always patent, and more or less dilated. We must remember, moreover, that this does not always refer to congenital occlusion in the strictest sense, since with justice those cases are also included in which the symptoms of closure of the duct have only made their appearance after birth, usually in the first days or weeks after delivery. If we start from the undoubtedly plausible and at least uncontroverted theory that, at one time, the bile-duct was permeable, we only need, in explanation of the occlusion developing at a later period, the assumption that, in consequence of a catarrhal and superficial, or a deeper-seated, more phlegmonous inflammation of the duct, the epithelium of the latter was thrown off, and its mucous membrane excoriated, so that the walls of the canal, being robbed of their protecting epithelial cover, may immediately unite with one another as far as they are in contact. In the hitherto observed cases no other cause for the closure of the bile-duct could be found, with the exception of inflammation of the latter. However, the fœtal inflammation of the bile-ducts, which has been taken for granted by us, has not been directly observed, but rather deduced from its sequences. Usually, also, we do not possess a plausible cause for such an inflammation. In this respect syphilis has been especially thought of, and the closure of the bile-ducts from perihepatitis has probably been looked upon as an analogous phenomenon. But a positive proof that

syphilis was the cause of the process leading to obliteration has not been definitely obtained in any of the cases in question. Moreover, perhaps some hereditary factor is involved; at least, the congenital closure of the bile-duct has been observed in several children belonging to the same family.[1]

3. *Closure of the biliary excretory ducts by tumors and new-growths of various kinds.*

The causal factors, which are included in this category, individually present a remarkable variety, and probably the majority of all cases of long-continued retention-jaundice, or those persisting until death, owe their development to them. In order to obtain a general survey, we will mention the factors in question according to their situation in the individual organs. We do not now take into consideration tumors of the liver, or, indeed, those cases of retention of bile caused by occlusion of the bile-ducts situated within the liver. It should be stated in advance that, with the exception of carcinomatous neoplasms (in the wider sense, and with the exception of multilocular echinococcus tumors of the liver), all the other growths which are here brought into question act in occluding the bile-duct by simple compression, although no further anatomical changes are produced in the bile-duct itself. The carcinomatous neoplasms, however, may as readily compress the bile-duct from without as they may grow into the wall itself, and narrow the lumen

[1] Cf. *Binz* (l. c.), and especially *West*, Diseases of Infancy and Childhood, 4 ed., 1859, p. 570. A not inconsiderable number of observations have been made concerning congenital closure of the biliary excretory ducts. In addition to the works of Donop, Binz, West, and Hirschsprung, which have been previously referred to under "Literature," we may also mention: *Lhommeau*, Bull. de la Soc. anatom., 1842; *Campbell*, Northern Journ. of Medicine for 1844; *Romberg* and *Henoch*, Klinische Wahrnehmungen, 1852, S. 188; *Wilks*, Path. Trans., Vol. VIII., p. 119; *Murchison*, Diseases of the Liver, 2 ed., p. 375; *Roth*, Virch. Arch., 43 Bd., S. 296; *Nunnely*, Path. Trans., Vol. XXIII., p. 152 (1872); *Morgan*, Med. Times, Feb. 16, 1878, p. 182; *Lotze*, Berl. Klin. Woch., 1876, No. 30, and Schmidt's Jahrb., 174 Bd., S. 265; *Wickham Legge*, Path. Trans., Vol. XXVII., p. 178; *John Glaister*, The Lancet, 1879, Vol. I., No. IX. (Mar. 1), p. 293. Of eight children of a healthy mother, the third, fourth, and fifth died with severe icterus after living barely a week; the sixth died after three weeks from hemorrhage of the funis, and was also deeply jaundiced. In the eighth child, who died in sixty-two hours from icterus, the autopsy showed marked stricture of the ductus choledochus in the neighborhood of its duodenal end.

somewhat like a cicatricial stricture, or fill the lumen of the canal.

Next to the cancerous tumors of the liver, gall-bladder, and other surrounding parts which reach the excretory duct in one way or another, and cause closure of the canal by one of the methods just mentioned, the cancers—primary as well as secondary—which start from the bile-duct, must be taken into consideration.[1] The rare primary cancers of the bile-duct usually grow as rugged or cauliflower-like masses into the lumen of the canal, fill it, and reduce it to a narrow slit, which is here and there entirely impermeable to bile. I have several times seen secondary cancers of the gall-duct appear in the form of a scirrhous infiltration, in which the walls of the canal, for the space of a few centimetres, were converted into a rigid mass, 4 to 5 mm. in thickness, the lumen, however, narrowed and slit-shaped or punctate, and entirely impermeable, at least for the bile. The latter cases correspond entirely, with regard to the mechanical relations of the occlusion, to simple fibrous stenosis of the bile-duct. I observed one case of scirrhous stenosis of the gall-duct by a neoplasm of sarcomatous nature (fibrosarcoma with small, round cells, very similar to lymphosarcoma).

The very emaciated woman, æt. forty-four years, with general dropsy, had presented an orange-yellow color of the skin for three to four weeks. Stools in the last two weeks entirely colorless. Death occurred from croupous pneumonia of the right upper lobe. Over two litres of brown serum in the abdominal cavity. The principal change consisted in a diffuse sarcomatous infiltration of the mucous membrane of the uterus and Fallopian tubes, the peritoneum and retroperitoneal lymphatic glands, the gastric mucous membrane, sarcoma nodules in the thyroid gland, pancreas, kidneys, etc. The liver very firm, but not granular. The ductus choledochus permeable throughout, entirely normal, its mucous membrane slightly tinged with bile. The cystic duct normal. The mucous and serous membranes of the walls of the gall-bladder infiltrated in spots with sarcoma. The hepatic duct, together with both hepatic branches, for a distance of about 1.5 ctm. from the point of bifurcation, is embedded in a firm mass of tissue, which is continued around the lumen as a layer, 1 ctm. in thickness. This new-formed tissue shows the same anatomical and microscopical appearances

[1] Cf. *Schreiber*, Ueber das Vorkommen von primären Carcinomen in den Gallenwegen, Berl. Klin. Wochenschr., 1877, No. 31; *Murchison* (l. c.), p. 397; *Bristowe*, Path. Trans., Vol. IX., p. 220, etc.

as the sarcomatous neoplasm in the uterus, peritoneum, etc. The lumen of the duct appears punctate upon transverse section, and permits the passage of a fine sound with difficulty; the mucous membrane in the region of the occluded spot is somewhat uneven, free from ulceration, although the separate coverings of the canal cannot be distinguished as individual layers. Immediately behind the occluded spot both hepatic ducts are dilated in the shape of ampullæ. The dilatation extends to the larger branches of these ducts, which will almost admit the little finger. The dilation rapidly grows less toward their radicles. The dilated portions of the ducts are filled with a dark green, very fluid bile. (The uterus was probably the starting-point of the neoplasm.)

Next to cancers of the duodenum—primary as well as secondary—are ranged the cancers of the excretory ducts. As soon as these tumors involve the posterior surface of the duodenum and that portion which is perforated by the end of the gall-duct, the latter is in danger of being occluded by the cancer in one or the other of the above-mentioned methods. Occasionally the occlusion only involves the point of entrance of the gall-duct, and then, at the same time, usually that of the pancreatic duct.

Tumors of the pancreas are also a relatively frequent cause of occlusion of the gall-duct. Among these the first rank is occupied by cancer of the head of the pancreas, which represents, as a rule, the primary tumor. As a matter of course, secondary or continuous cancers of the pancreas, or the not extremely rare lymphosarcomatous infiltration of these glands, will have the same effect when they correspond to them in size and position. The position of the ductus choledochus, with regard to the head of the pancreas, is not without influence upon the effects of these tumors on the gall-duct, as the latter will, under similar circumstances, be more endangered, when it penetrates the head of the pancreas, than when it is only applied externally to the latter.[1] Cancer of the head of the pancreas may surround the ductus choledochus, spread to the walls of the duct, infiltrate it, and thus stenose its lumen, or finally it may burst into the canal and occlude the duct at any portion of its course. When the cancer of the head of the pancreas is of very considerable dimensions,

[1] According to *Wyss*, l. c. (Virch. Arch. Bd. 36, S. 454), the ductus choledochus passes in about one-fourth of the cases through the substance of the pancreas, and in about three-fourths merely alongside the latter.

it may produce compression of the gall-duct, in case this merely passes alongside the pancreas, without drawing it together or filling its lumen. Finally, cancer of the head of the pancreas may extend to the duodenum, and thus lead to closure of the mouth of the gall-duct.[1] It is evident that the pancreatic duct is also in danger of occlusion in all such cases. It occurs exceptionally that some other (non-carcinomatous) tumor of the head of the pancreas causes occlusion of the gall-duct. Wyss[2] describes a remarkable case, in which a dilatation of the ductus Wirsungianus gave rise to complete occlusion of the end of the ductus choledochus, and produced jaundice of four months' duration.

Enlarged lymphatic glands in the transverse fissure, and in the course of the hepato-duodenal ligament, are a relatively frequent cause of simple compression of the biliary excretory ducts and of mechanical jaundice. The enlargement of the glands in question is due most frequently to cancerous, more rarely to tubercular, cheesy, amyloid or lymphosarcomatous[3] degeneration. In many cases of jaundice in cancer and amyloid degeneration of the liver, the icterus is caused by a similar affection and enlargement of the portal lymphatic glands. In such cases the compression often involves, at the same time, the trunk of the portal vein, and thus gives rise to ascites.

Cancer of the stomach occasionally gives rise to the production of retention of the bile, more rarely from the pressure exercised directly by the tumor upon the gall-duct, more often, however, indirectly from the pressure produced by secondary deposits of cancer in the portal lymphatic glands or omentum.

It is said that large tnmors of the (right) kidney are capable of producing jaundice by compression of the biliary excretory duct (Copland, quoted by Murchison, l. c. p. 355). *A priori* the possibility of such an occurrence cannot be disputed; at all

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[1] Cf. among others, cases 6 and 7 in *Frerichs*, l. c., I., S. 146 ff, and various others in *Murchison*, l. c., S. 380 ff.

[2] L. c., S. 455.

[3] *Murchison* (Path. Trans. Vol. XX.) reports the case of a girl æt. thirteen years, in whom permanent jaundice was caused by a lymphosarcoma of the portal glands, inasmuch as the considerably enlarged glands compressed the gall-duct.

events it must be regarded as an extremely rare occurrence that tumors of the kidney should have the effect referred to.

A striking example of the difficulty with which closure of the bile-ducts and jaundice are produced by tumors of the kidney, is shown by the following case recently observed by me in a girl æt. seventeen years, who had suffered for a year from a tumor in the region of the right kidney. The autopsy revealed an ovoid tumor, enclosed in a firm fibrous capsule, belonging to the right kidney, and in which this organ had been destroyed without leaving a trace. The tumor is more than 30 ctm. long, about 20 ctm. wide, and of like thickness, about nine pounds in weight, extends to the pelvis, and projects 4 ctm. beyond the median line of the abdomen. It is found to be a myxoma hemorrhagicum; the original myxomatous tissue is only retained in small spots, otherwise it has become entirely indistinguishable on account of old and recent hemorrhages. At the upper extremity the capsule of the renal tumor has been perforated, and through this opening the latter has extended to the right lobe of the liver, not alone pushing the latter upward, but at the same time compressing its upper lobe so that it was converted into a sac hardly 1 ctm. in thickness, covering the masses of myxoma half as large as a man's head, which project from the upper end of the renal tumor. The other lobes of the liver are well preserved and pushed to the left. The apex of the diaphragm stands, on the right side, at the level of the first intercostal space, on the left at the height of the fourth rib. The right lung entirely compressed. The new-growth, which has also pressed itself into the right lobe of the liver, extends exactly to the transverse fissure which is pushed to the left and upward. All the bile-ducts are free and permeable, but markedly dilated. The gall-bladder only contains a small quantity of viscid colorless mucus. Marked jaundice has never occurred (nor ascites); at times, however, a slight icteric color of the skin has been noticed. For a long time worm-shaped clots of blood had been passed in the urine.

Tumors of the omentum of a cancerous, colloid cancerous, or tubercular nature, as well as so-called retroperitoneal tumors, may occasionally attain such a distribution that they finally surround the gall-duct and compress it to entire impermeability.[1] As a rule, however, the starting-point of such tumors can only be determined with great difficulty during life.

Aneurisms are a very rare cause of compression of the gall-duct and of retention-jaundice. Aneurisms of the abdominal aorta, especially, can only compress the gall-duct when the sac has attained colossal dimensions. A case of this kind was ob-

[1] Cf. *Bristowe's* cases in Path. Trans. Vol. IX., p. 225, and Vol. XVII., p. 136.

served by Hutton ;[1] the sac extended from the ridge of the ilium to the lower end of the scapula. Aneurisms of the hepatic artery give rise somewhat more frequently to jaundice, but it is precisely these aneurisms which are of very rare occurrence. Among five cases of this kind which are found compiled in Frerichs,[2] more or less marked jaundice was noticed in three. Jaundice appears to have been very rarely observed in aneurisms of the superior mesenteric artery.[3] Gairdner[4] reports a case, in which jaundice was produced by an aneurism of the superior mesenteric artery, which opened into the duodenum, and had caused repeated profuse hemorrhages, like those in perforating ulcers of the stomach.

It is a positively demonstrated fact that retention-icterus may be caused by the pressure exerted upon the biliary excretory duct by a large accumulation of firm fæcal matter in the intestines, by the uterus in the last stages of pregnancy, or, finally, by very large tumors of the ovaries or uterus (ovarian cysts, myo-fibromata of the uterus, and similar growths). It is also known, however (and this is readily understood), that the above-mentioned factors only have such an effect in relatively very rare cases. In fæcal tumors and in pregnancy, in which the jaundice does not usually last very long, further consequences of the closure of the bile-duct than this temporary retention-icterus will hardly be produced.

Finally, the fact, which has been especially brought into prominence by Niemeyer, must be mentioned, that certain changes in the position of the liver, especially when, in addition, perihepatitic adhesions of its inferior surface with adjacent organs or warty and cord-like thickenings of its serous covering are present, will cause a bending of or dragging upon the bile-ducts situated outside of the liver, and may thus give rise to impermeability of the latter, and to retention-jaundice. Virchow[5] has called attention to similar conditions during pregnancy, etc.

[1] *Stokes*, Diseases of the Heart and Aorta, 1854, p. 633.

[2] Klin. d. Leberkrankhtn. II. S. 359.

[3] Cf. *Wilson's* case, Medico-Chirurg. Trans., Vol. XXIV., p. 221.

[4] Clinical Medicine. 1862, p. 504.

[5] *Vide* his Gesammelte Abhandlungen. Frankfurt a. M., 1857, S. 756 u. 777; also Virch. Arch. VIII., S. 360, and Deutsche Klinik. 1854. No. 4.

Pathological Anatomy.

As we have already described, so far as is necessary, the anatomical changes at the point of occlusion in enumerating the etiological factors, it only remains now to discuss those changes, which develop later in the biliary apparatus, as soon as the excretory duct has become impermeable. The immediate consequence of the occlusion is naturally an interference with the flow of bile and retention in those portions of the canalicular system situated behind the point of occlusion. The retention of bile gives rise to a progressive dilatation of the affected canals, which at times attains a truly enormous grade. If the obstruction is situated in the ductus choledochus, the gall-bladder will also take part in the dilatation, provided the cystic duct is permeable. If, however, the hepatic duct is closed, the dilatation will only extend to those bile-ducts situated within the liver. Those portions of the canals situated in front of the point of occlusion present, in the main, a normal appearance; they are empty or contain some colorless mucus.

The anatomical sequences of closure of the gall-duct are best observed in those cases in which the obstruction is situated at the duodenal end of the ductus choledochus, for instance, when complete atresia has been caused by inflammatory adhesion of the walls of the duct. The bile-ducts outside of the liver are dilated in various degrees, at the same time elongated,[1] and therefore bent and twisted like a loop of intestines. In the most severe cases the ductus choledochus, which is filled to distention, appears somewhat like a well-filled loop of the small intestines, and its diameter is increased to 5–6 ctm. The end of the duct (which is shaped like a blind sac) is sometimes pushed like a peg into the cavity of the duodenum. The hepatic duct attains the

[1] In one case of this kind I found the biliary excretory duct 21 ctm. long from the union of both hepatic ducts to its blind sac-shaped termination, 1 ctm. from the porus biliarius; of this, 8 ctm. belonged to the hepatic duct, and 13 to the ductus choledochus. The diameter of the latter amounted to 5 ctm.; the cystic duct was 5 ctm. long, its walls were on the average only 1.5 ctm. in thickness, but were, in many places, hollowed out into niches, and these depressions were so wide that a medium-sized cherry could be placed in them.

same width, and each of its two chief branches will readily admit one or two fingers; the other branches within the liver correspond, on an average, to about the thickness of the little finger. Gall-ducts of this width can be seen penetrating even to the surface and into the extreme sharp edges of the liver. The dilated gall-ducts present either a simple cylindrical shape, or they are provided with numerous shallow and ampulla-shaped recesses. The cystic duct, in case this is patent, attains a diameter of from 1 to 2 ctm. With the same proviso, the gall-bladder appears enormously enlarged but normal in shape. In one case under my observation it contained almost one litre of fluid, was more than 20 ctm. long, and more than 10 ctm. thick at the fundus. It, therefore, projects beyond the lower border of the liver, as an oval hemispherical tumor, by perhaps ten or more ctm., and then lies upon the right brim of the pelvis. The walls of the large bile-ducts and gall-bladder appear, in comparison with the marked dilatation, relatively not inconsiderably thickened. The mucous membrane of the gall-ducts is smooth, provided with shallow, ditch-like recesses, which correspond to the mouths of the glands of the ducts.

During the first period after the retention of the bile, the liver is enlarged, its circumference sometimes attains twice the normal dimensions. After long continuance of the retention it again grows smaller and may finally be perceptibly less than the normal size. The hepatic tissue is of a dark olive green, indistinct acinous appearance, extremely anæmic, flaccid, but at the same time more resisting, and more difficult to cut on account of the often considerable increase of the interstitial connective tissue, which usually develops in consequence of the occlusion of the gall-duct.[1] Vesicular or cord-like projections are present here and there upon the surface of the liver, especially in the vicinity of its sharp borders, corresponding to the dilated biliary canals, above which the parenchyma of the liver has entirely disappeared.

The fluid, which is found in the dilated gall-ducts, varies very considerably in amount. In very high degrees of dilatation the

[1] Cf. *Charcot* and *Gombault.*

bile-ducts in their entirety may contain almost one litre of fluid, and occasionally perhaps even more; the gall-bladder will hold about the same quantity. We possess histories, however, dating from former times, according to which the quantity of fluid accumulated in these canals must have been even much larger.[1]

There are decided differences with regard to the nature of the fluid in question and its chemico-physical reactions, according to the duration of the occlusion of the bile-duct. In the beginning, of course, the fluid which accumulates in the canals is pure bile, *i.e.*, a yellowish brown, quite thin substance. The bile then becomes mixed with a mucoid secretion produced by the mucous membrane of the gall-ducts upon its surface, and also by the mucous glands imbedded in it. If, however, the flow of bile has been prevented for a long time, for several weeks or months, we find the gall-ducts no longer filled with a fluid like bile, but with a clear substance, which possesses a very light, pale glass-green color, and is more or less mucous, the consistence of which reminds us, therefore, of thin synovia. The very small quantities of specific constituents of the bile, which are present in a fluid of this character, at length disappear entirely. We finally, then, find the bile-ducts filled with a perfectly colorless substance as clear as crystal, or a more or less mucoid, thin fluid, which is slightly opaque from mixture with mucus, and which, notwithstanding the most intense jaundice of the liver and of other tissues, contains no trace of bile. In this stage we speak of sacculated dropsy of the biliary passages (hydrops ductuum biliarium saccatus). This term appears to be especially appropriate in the cases in which a perceptible atrophy of the hepatic tissue also occurs, as in Brierre Boismont's often quoted case.[2] In a man æt. fifty years, the ductus choledochus was contracted in its middle by a warty band formed of the hardened Glisson's capsule; the canal was as wide as the small intestine. The liver of a dark green color,

[1] In *Frerichs* we find quoted *De Jonge* (Philos. Trans. T. XXVII.), who is said to have observed 7 pints, and *Van Swieten*, 8 pints, *i.e.*, about 4–4½ litres of bilious fluid in the gall-bladder. *Frerichs* himself did not find more than 8–16 ounces, *i.e.*, ¼–½ litre in the gall-bladder.

[2] Observations sur quelques maladies du foie. Arch. gén. T. XVI., p. 38.

its tissue completely atrophied so that it only represented a large fluctuating cyst.

The connection between the biliary canals and the parenchyma of the liver must be regarded as completely destroyed in this sacculated dropsy. The mucous membrane of the canals now forms a cyst-wall, which is completely closed; if any bile should still be produced, it can no longer pass into the bile-ducts, while their original biliary contents are absorbed and replaced by large quantities of a sero-mucous fluid, the product of the secretion of the mucous membrane of these canals. If this condition lasts for a long time, the mucus present also disappears gradually, and the fluid assumes a purely serous character. Frerichs, with justice, regards the fact that the contents of the gall-ducts appear colorless, notwithstanding the jaundice which is present at the same time, as a proof that the mucous membrane of the canals has no part in the separation of the biliary matters from the blood.

In a case[1] in which the mouth of the ductus choledochus had been entirely closed for nine weeks by a cancer of the duodenum, Frerichs made a chemical examination of the colorless and almost clear fluid with which the gall-ducts were found filled to repletion. It had a faint alkaline reaction; it showed no trace of reaction for biliary coloring matter upon the addition of nitric acid, nor could any of the biliary acids be demonstrated by Pettenkofer's tests. The fluid consisted of 98.20 per centum of water and 1.80 per centum of solid constituents, of which 0.65 were organic matters (mucus, etc.), 0.07 soluble alkalies, and 0.08 per centum insoluble earths.

Although the dilatation of the bile ducts often attains an astonishingly great intensity, it nevertheless only leads in extremely rare cases to rupture of their attenuated and greatly dilated walls. The development of the rupture, which has been observed in the gall-bladder and the common excretory duct[2] as well as in those canals situated within the liver, is greatly favored by gross violence acting from the outside, such as a blow upon the

[1] Klin. d. Leberkrkhtn., I., S. 146 ff. Case 6.

[2] *Wolf* describes a case of complete transverse rupture of the common excretory duct. Gaz. méd. de Paris, 1830.

abdomen, etc., or by pathological processes which are situated in the walls of the bile-ducts, such as inflammations, ulcerations, etc. Rokitansky [1] states that repeated ruptures of the smaller biliary canals and the formation of more or less extensive extravasations of bile into the liver occur in many cases of retention of bile. While no special significance is to be attached to this process, the rupture of biliary canals situated outside of the liver leads to flooding of the peritoneum with biliary fluid, and in all cases to rapid death from general peritonitis.

The microscopical examination of the liver furnishes weighty data with regard to the condition of the secretory parenchyma. In the first place, it confirms the more or less considerable increase of the intralobular connective tissue, which had been previously recognized by the naked eye. In the cases which I have examined—among which were some in which the flow of bile had entirely ceased for a number of months—I always found the liver-cells well preserved on the whole, the larger number of them being of medium size; in spots, however (in which special local influences may have been at work), they are smaller and decidedly atrophic. The liver-cells are not alone diffusely bile-stained, but they also contain biliary coloring matter in granular form, and even small scattered crystals of bilirubin are present in the tissues. The liver-cells are usually free from fat in the form of larger drops, the protoplasm, on the other hand, is in a condition of cloudy swelling, and the nucleus of the cell is, therefore, not so prominent. The connection of the hepatic cells with one another appears to be loosened; they are less regularly arranged than in the normal condition. These changes, therefore, correspond to subacute or chronic parenchymatous hepatitis. Granular disintegration of the liver-cells as an outcome of parenchymatous degeneration, such as is characteristic of acute yellow atrophy of the liver, does not appear to occur, at least to any great extent. The statement by Budd, who maintained this view with regard to certain cases, had been discarded by Frerichs [2] as untenable. Partial destruction of the parenchyma of the liver undoubtedly occurs from various causes, but so

[1] Lehrb. d. pathol. Anat., III., S. 364.

[2] L. c. I., S. 125. Note.

gradually that sufficient time elapses for the absorption and removal of the degenerated material. Bile-stained, homogeneous, slightly transparent plugs of inspissated bile of a peduncular, knotty, here and there branching shape, or rounded, somewhat larger lumps of the same substance and of a similar appearance, are found in many places within the capillary bile-ducts between the liver-cells. The finest interlobular ducts present no special deviation apart from the bile-staining of their tissue, especially of the epithelium, nor do they appear perceptibly dilated. In the larger bile-ducts, to which the dilatation extends, the epithelium is said to become flattened in time, and short cylindrical or even pavement epithelium is found instead of the elongated cylindrical cells which were originally present.

We must, therefore, entertain the following idea with regard to the functional and anatomical condition of the liver in long-continued cessation of the flow of bile:

After the occlusion of the excretory duct has occurred, the formation of bile at first occurs as before, but the secretion is dammed back in the bile-ducts, the latter dilate and thus produce, for a long time, a progressive increase in the size of the liver. Absorption of the retained bile occurs from the beginning of the retention, and the hepatic tissue itself is exuberantly impregnated with it. The formation of bile in the hepatic cells and the absorption of the portion dammed back in the ducts occur concomitantly for a long time and in such a manner that the quantity absorbed within a certain time is not much less than that produced. A period now arrives in which the liver again diminishes in size; this period continues until death, which eventually occurs. As the volume of fluid contained in the bile-ducts has, at least, not diminished during this time, the reduction in the size of the liver must be due to disappearance of hepatic tissue. This disappearance is due, in a minor degree, to the pressure exercised upon the hepatic tissue by the later retraction of the interlobular connective tissue which has hypertrophied as the result of the occlusion of the bile-duct; in the main, however, it is caused by the pressure to which the parenchyma is subjected by the enormously dilated gall-ducts. Diminution of the production of bile goes hand in hand presumably with the atrophy of the

hepatic tissue, and indeed the gradually developing parenchymatous degeneration of the liver-cells, which must be regarded, at least in part, as the result of the continued saturation of these cells with biliary constituents, appears to diminish the secretory function of the parenchyma so considerably in the later stages of the disease, that the formation of bile, in individual cases, may be regarded as entirely interrupted. The proof of this statement can be obtained in the pathology of occlusion of the bile-duct, especially from the appearance of jaundice toward the end of the course of the disease and from the so-called cholæmic (nervous) symptoms developing in this stage. The disappearance of specific constituents of the bile from the fluid contents of the dilated gall-ducts is not directly connected with the abolition of the formation of bile. This may occur even though the liver-cells still produce bile, the undisputed premise being granted that the secretion, which is still furnished by the liver-cells, is immediately taken up by the hepatic lymphatic vessels, without passing into the gall-ducts, and is conveyed into the general nutritive fluids of the body.

Other anatomical changes, which might be looked upon as due to closure of the biliary excretory duct, are not found in the bodies of those who have died from this condition, with the exception, naturally, of the general emaciation, the icteric color, and marked anæmia of the various organs, together with the hemorrhages into the tissue of the external integument, the mucous membranes, etc., which must be attributed to the cholæmia. At the most, attention should be called to the condition of the kidneys, which is especially important with regard to the course of the disease, and which are found saturated with biliary coloring matters, and frequently in a condition of parenchymatous degeneration, *i.e.*, swollen, anæmic, flaccid, and of softer consistence.

Pathology.

General Clinical History.

The general clinical history occurring in occlusion of the biliary excretory duct is in itself very characteristic, but is variously modified by the symptoms which are due to the causal dis-

turbances to which the occlusion is due. There is no occasion for entering, in this place, into a consideration of the latter. We will therefore only discuss those cases in which the causal disorder, giving rise to the occlusion, runs a latent course and the symptomatology of the stenosis of the bile-duct is presented unmixed with any foreign characters.

In such cases the beginning of the disease is marked by the appearance of jaundice, which either develops gradually, and only attains great severity after the lapse of several weeks, or becomes very intense during the first few days. Usually the jaundice soon attains its greatest intensity; the primary citron or saffron yellow color of the skin passes into a brown, bronze-like, and finally, into a dark olive-green (melasicterus), and continues in this manner until the end of life, with no very considerable variations. The yellow color of the skin goes hand in hand with the symptoms of gastric and intestinal catarrh: digestive disturbances of various kinds, especially anorexia, antipathy against meat and fatty food, frequent eructations, nausea, feeling of pressure and fulness in the region of the stomach. The evacuations are retarded, and there is marked flatulence. The passages from the bowels are either entirely colorless from the beginning, or they, at least, soon become so; they present an appearance like clay, and have a disgusting odor. In the first weeks of the disease a feeling of tension, or even a certain degree of swelling becomes noticeable in the hepatic region—symptoms which may again be lost during the further course of the disease. The patient is annoyed by severe, protracted, and often intolerable pruritus of the integument, which even interferes with rest at night, and prevents sleep. Then follow the symptoms of the hemorrhagic diathesis: hemorrhages from the nose and gums, bloody admixture in the passages, numerous ecchymoses, and bloody suffusions in and under the skin, which disappear, and are then always replaced by fresh ones. After an approximately equal duration of all these symptoms, and after the condition has lasted several weeks, or even months, the signs of a general disturbance of nutrition become noticeable: the patient emaciates to a striking degree, the skin is thin and dry, the adipose tissue and muscles disappear, the energies of the body become

lost more and more, marked marasmus and severe cachexia develop. Dropsical swelling of the feet becomes visible, and, under certain circumstances, ascites occurs. Febrile symptoms do not develop during the entire course of the disease, unless some special exciting cause is present independent of the closure of the bile-duct. Thus, without any change for the better, the patient dies, after the disease has lasted for several months, or even a couple of years, unless an earlier termination is brought about by the affection which lies at the bottom of the occlusion of the bile-duct, or by some accidental intercurrent disease, such as pneumonia, pleurisy, etc. During the last days of life the symptoms of so-called cholæmic intoxication also usually set in: the patient becomes apathetic, sleeps a great deal, his head feels dull, he is roused from sleep with difficulty, consciousness is disordered, and he finally sinks into coma, which continues until death.

Symptomatology.

Jaundice, with all its attendant symptoms, constitutes by far the most predominant element in the clinical history produced by occlusion of the common bile-duct. Its most characteristic symptom, viz., the yellow color of the skin, passes, in those cases in which the occlusion develops gradually, correspondingly slowly, in suddenly developing occlusion more rapidly, into the deeper, more saturated tints (bronze-brown and dark olive-green), and thus reaches—especially in very thin and sapless individuals—the most extreme degrees which are ever brought to our notice. The yellow color of the skin is not only permanent, but it also maintains, after it has attained its acme, the height which has been reached, and any variations usually remain within narrow limits. If marked clearing of the color of the skin is observed, despite continued occlusion of the bile-duct and complete discoloration of the fæces, this must be regarded as an unfavorable sign, since it would show that the formation of bile is lessened, and the function of the liver markedly disturbed, perhaps entirely abolished.

The exciting cause is the disappearance of the parenchyma of

the liver, which usually occurs after long continuance of retention of bile, and, perhaps, even more, the progressive degeneration of the hepatic tissue, which is still present. In a few cases the most intense grades of jaundice are found to disappear almost entirely, although the complete discoloration of the fæces permits no doubt with regard to the continuance of the occlusion of the bile-duct. In these cases, then, the production of bile must be entirely suspended, yet this condition may persist for a long time, and even for several months.[1] It lies in the nature of the case that the clearing or disappearance of the icteric color of the skin belongs especially to the latter stages of the course of the disease, even though it cannot be maintained that this always forebodes the approach of the fatal termination.

In addition to the yellow color, the external integument also often presents other morbid symptoms, as chronic icterus is usually combined with severe pruritus of the skin, which continues obstinately, annoys the patient extremely, and often becomes unendurable. As a rule, the pruritus appears at once upon the development of the icteric color of the skin, or is quite soon combined with it. In a few cases it continues, like the jaundice itself, with almost undiminished violence, until death; sometimes it diminishes considerably, or disappears entirely for a time, to reappear at a later period. The pruritus is often diffused over the entire body; its chief seat, however, is upon the inner surface of the hand, the soles of the feet, and between the toes; in degree it is also usually most severe.

It increases at night, in bed or in a warm room, the patient unavailingly scratches the skin, the pruritus even robs him of sleep. As a rule, a true exanthem of definite form is not noticeable; the scratched portions of skin become covered with brownish scabs. In rare cases, a prurigo-like papillary eruption, an urticaria or lichen develops, and the formation of furunculi and

[1] *Vide*, among others, the remarkable case of *Heitz* (Berl. Klin. Wochenschr. 1876, Nos. 6 and 7): the patient, about seventy years old, although suffering from complete occlusion of the ductus choledochus by a large gall-stone, was only temporarily jaundiced during an illness of three years' duration, the stools, however, being, without interruption, entirely discolored. Constituents of the bile could not be demonstrated in the urine during the period in which he was free from jaundice.

similar localized inflammations of the skin may occasionally occur as an effect of chronic icterus.

The most remarkable affection of the skin, however, which sometimes develops in chronic jaundice, is the so-called xanthelasma[1] (Erasmus Wilson)—pale yellow spots or slightly prominent plaques, which develop at first upon the eyelids, then also upon other portions of the body in the skin, mucous membranes, etc. Usually the eruption only appears after the jaundice has lasted for several months and almost always begins in the eyelids. In the later stages of the disease the xanthelasma also appears in its tubercular form. After Hilton Fagge had maintained that xanthelasma is peculiar to milder cases of simple icterus, Moxon[2] and Wickham Legg[3] have reported cases in which it was observed in cicatricial stenosis of the ductus choledochus.

Next to the appearances on the part of the external skin, the symptoms referable to the digestive tract chiefly occupy the foreground in chronic icterus. It is to be expected, *a priori*, that the function of these organs will be markedly interfered with in continued abolition of the flow of bile into the intestine, since although the bile is not absolutely necessary in digestion, it nevertheless exercises the greatest influence upon its completeness. Retention of bile is, as a rule, combined with loss of appetite and all kinds of disturbances of digestion. The tongue is usually unclean, covered with a thick, greasy, brownish gray coating; the patient complains of a disagreeable, bitter taste in the mouth, and various abnormal gustatory sensations of other kinds. Nausea and a tendency to emesis are especially present in the morning after waking. The loss of appetite often increases to the most extreme antipathy against food, especially against meat, fatty articles, etc. The patient longs mostly for fresh vegetables, and highly spiced, irritating substances. Digestion is delayed, the epigastrium distended, there are frequent sour eructations, large development of gas in the intestines, and escape of foul-smelling wind. Dulness of the head, headache, and other symptoms of this character are also present.

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[1] A quite detailed description of this affection is contained in *Strauss*, Des ictères chroniques, p. 90.

[2] Path. Trans., 1873.

[3] Ibid., 1874.

However, all the above-mentioned digestive disorders may remain absent. There are cases of permanent icterus in which the appetite remains excellent, in which it may even be excessive and true bulimia develops—as in dogs in whom a biliary fistula has been made—in which, finally, digestion, although not perfect, occurs without any noteworthy disturbances. And this may continue not alone for months, but even for years.

Careful attention must be paid to the constitution of the stools during the entire course of the disease, since they alone, by their color or discoloration, can give us positive information whether the gall-duct is closed or is open at intervals (as, for instance, when a gall-stone in the ductus choledochus changes its position). Constipation is generally present, but it is usually not very obstinate, inasmuch as it can be readily relieved by treatment. If we consider their firm consistence, the stools are very profuse, especially in patients with a good appetite. The fæces have lost their color, are whitish gray or clay-colored, with a very fetid odor, sometimes moulded, sometimes like a thick porridge. The discoloration continues until death, unless a temporary greenish or brown color is produced accidentally in consequence of the use of certain drugs (calomel, rhubarb, etc.). But even apart from this and despite absolute retention of bile, colored stools may occasionally appear, their color being due to admixture with blood. As the tendency to hemorrhages is peculiar to icterus, stools which are colored dark by blood do not occur so rarely. In Osborne's opinion, the icteric-colored secretion of the intestinal glands would suffice to stain the fæces despite the absence of the flow of bile into the intestines.

Not infrequently, also, the passages from the bowels show an unusually large quantity of fat, and, indeed, true stearrhœa is sometimes present. This symptom is especially manifested in those cases in which the occlusion of the ductus choledochus is combined with that of the pancreatic duct, as, for instance, in cancer of the head of the pancreas, as the fat-digesting and fat-absorbing function, not alone of the bile, but also of the pancreatic juice, then disappears. But an abnormal amount may also be observed in the fæces when the ductus choledochus is alone occluded.

The examination of the urine is important in the diseased conditions under consideration, for the reason that upon the kidneys devolves almost exclusively the function of freeing the blood from the biliary constituents with which it is continually being surcharged. In icterus the kidneys must do duty for all that is neglected on the part of the liver and the biliary apparatus. After long duration of the jaundice a sort of equilibrium will develop in which about the same amount of the specific constituents of the bile are excreted by the kidneys in the urine as were formed in the liver and passed into the blood during the same time. If, however, as often occurs toward the end of the disease, the function of the kidneys is disordered while bile is still being formed, the quantity of biliary constituents in the blood will reach a threatening height and the signs of cholæmic intoxication will develop.

From the beginning, the dark, intense brown color of the urine attracts attention, and this passes into a blackish brown and brownish green as the jaundice increases. By means of Gmelin's reaction we can determine the presence of biliary coloring matters in the urine, and that of biliary acids by Pettenkofer's tests. As with regard to the yellow color of the skin, similar variations occur in the quantity of pigment and biliary acids which the urine contains, although there is no change in the occlusion of the gall-duct; this also reflects the energy of the hepatic function, or of its abolition.

The daily amount of urine, as well as its specific gravity, vary within very wide limits according to accidental external circumstances. In very severe grades of icterus a marked diminution in the quantity of urine may occur toward the fatal termination, and may be explained by the obstruction of numerous uriniferous tubes in the kidneys by granular masses of biliary coloring matter (Moebius). The reaction of the urine is usually faintly acid. After Meissner had attributed to the liver an important rôle in the formation of urea, it had been supposed that a diminution in the absolute quantity of urea should be observed on account of the lowered activity of the liver accompanying occlusion of the bile-ducts. But it has been shown that the formation of urea is influenced by very complicated factors, and that it

does not, by any means, run simply parallel with the activity of the liver. The quantity of urea excreted daily is, indeed, often diminished in jaundice of long duration, sometimes, however, it is normal, or even increased, although the reasons therefor cannot always be detected. Albumen does not occur constantly in the urine of those suffering from jaundice, and, as a rule, is only present in small quantity; it only increases in amount toward the end of life with the increase in the parenchymatous and fatty degeneration of the kidneys. According to Nothnagel[1] casts appear in the urine in every severe case of jaundice, when the urine also contains biliary acids at the same time; they are few in number. The casts are chiefly hyaline, covered with small shining granules of a yellowish color and with a few bright yellow epithelium cells. However, Nothnagel only found albumen in the urine in the minority of cases; its quantity was usually in inverse proportion to the number of casts.

According to Moebius,[2] the glomeruli of the kidneys are found entirely free from bile-pigment after intense jaundice has lasted for months. On the other hand the epithelium of the convoluted tubes and Henle's loops are of a golden yellow color, filled with pigment granules, and yellowish plugs of a brittle, granular character (bile-pigment casts) are situated in the lumen of these canals. The larger part of the pigment is found in the ribbon-shaped canals and the excretory tubes of the pyramids; the epithelial affection here retires into the background, the filling of the lumen, on the other hand, steps into the foreground. In addition, hyaline casts, partly yellowish, partly colorless, are present in the uriniferous tubes. The more intense and prolonged the jaundice, the larger is the number of uriniferous tubes affected by the infiltration of pigment, the tougher and darker are the pigment masses, and the more the process extends to the termination of the renal tubes, the collecting-tubes of the pyramids. In icterus, therefore, there is a true pigment infiltration (not merely imbibition) of the kidneys. Icterus, as such, appears, according to Moebius, to lead to parenchymatous degeneration of the kidneys, which is perhaps directly due to the presence of biliary acids. The parenchymatous and fatty degeneration of the epithelium is shown by the presence of albumen and exudation casts in the urine. The obstruction of numerous excretory tubes by firm masses of bile-pigment may diminish the quantity of urine considerably in severe grades of icterus.

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[1] Ueber Harncylinder beim Icterus, Deutsch. Arch. f. Klin. Med. XII., S. 326.

[2] Ueber die Niere beim Icterus. Arch. d. Heilk. XVIII. 1877, S. 83.

We may mention as the most important symptom, on the part of the circulatory apparatus, the diminution in the frequency of the pulse, which is to be attributed to the biliary acids present in the blood. The frequency diminishes from 78–80 beats to 50, 40 and less; Frerichs (l. c. I., p. 116) counted in one case only 28, and in another only 21 beats per minute. This diminution of frequency continues sometimes for a long, sometimes for a short period. If fever, by chance, supervenes, the the number of beats increases, but not to the same extent as it would were not icterus present at the same time. But the diminution in the frequency of the pulse is not by any means a constant phenomenon in icterus; it is often absent during the entire course of the disease, although we are not therefore warranted in the inference that, under such circumstances, no biliary acids are taken up by the blood, as it is well known that these acids rapidly undergo decomposition and chemical changes in this fluid. In other respects, the pulse is usually soft, small, readily compressible, the arterial tension is therefore diminished; the opposite condition constitutes the exception. The impulse of the heart is weak and sometimes irregular.

Potain and Gaugolphé [1] recently called attention to a peculiar cardiac murmur, which is attributable to the icterus, the significance of which has not, however, been definitely determined (cf. Strauss, l. c., p. 110).

In severe and long-continued icterus, in consequence of occlusion of the bile-duct, the nervous system is markedly affected in almost all cases. Aside from the pruritus of the skin previously referred to, and from the symptoms of cholæmic intoxication which will be discussed at a later period, we must call attention to the morose, at times irritable, at times apathetic condition and the hypochondriacal mood of such patients. They are, moreover, incapable of prolonged work, their energies are rapidly exhausted, the slightest exertion is disproportionately difficult for them. Xanthopsia, which is a very rare symptom, has been occasionally observed also in chronic icterus, in consequence of permanent occlusion of the bile-duct, and usually disappears very rapidly.

[1] Du bruit du souffle mitral dans l'ictère. Thése de Paris, 1875.

Among the constitutional symptoms in the clinical history of permanent occlusion of the bile-duct which must also be attributed to the icterus, the general emaciation of the body and the tendency to hemorrhages assume a prominent position. The emaciation and progressive weakness are satisfactorily explained by the variously disturbed and incomplete digestion, which results from the continued absence of bile in the intestines. It becomes noticeable quite soon in very small children; in older individuals a number of weeks usually elapse before it develops in a marked manner. The condition of the appetite, of course, possesses great influence in this respect. Some patients, who have a good appetite, even maintain for years their previous condition of good nutrition. Finally, true marasmus develops with a high degree of weakness and dropsical swelling of the lower extremities. Any ascites which may be present is explained by local causes, and the change which gives rise to occlusion of the bile-duct may also exercise pressure upon the portal vein.

The signs of a hemorrhagic diathesis will rarely be missed in the long-continued icterus, which is due to occlusion of the gall-duct. In many individuals, especially in very small children, the tendency to hemorrhages makes itself felt soon after the beginning of jaundice; in others only after it has continued for a long period, and at times it only appears shortly before the occurrence of the fatal termination. It manifests itself by spontaneous, frequently repeated epistaxis, by hemorrhages from the softened gums, the mucous membrane of the buccal cavity, by ecchymoses into the skin and conjunctiva, or by bloody streaks and suffusions in such portions of the skin which are subjected to pressure, even though very slight. Hemorrhages from the gastric and intestinal mucous membrane (especially the rectum), and hemorrhages from the funis in very small children, are also observed, and at times even attain a threatening severity, which, at all events, hastens the decline of the organism. In the dead subject ecchymoses are also found in the muscular tissue of the heart, the serous membranes, and in other organs.

Febrile symptoms, rise of temperature, etc., do not occur primarily in closure of the bile-duct during the entire duration of this condition, unless the retention of bile is combined with

an intense inflammation of the biliary passages, such as occurs especially when gall-stones or other foreign bodies in the biliary canals are present at the same time, more rarely under other circumstances. In such an event, the fever presents a strongly remittent or perhaps intermittent type, so that it may even be mistaken for intermittent fever. Charcot has framed the hypothesis that the fever develops from the absorption of bile, with which inflammatory products from the walls of the biliary canals have been mingled, in the same manner that, in cystitis from retention of urine, the fever develops from absorption of purulent urine.

The local symptoms on the part of the liver and the biliary apparatus, which are due to the closure of the bile-duct, fall into the background when compared with the sum of icteric symptoms. During the first period of the disease an enlargement of the liver is demonstrable, and is caused, in the main, by the enormous dilatation of the bile-ducts situated in it. In the normal position of the diaphragm the lower border of the liver projects from two to four fingers'-breadth beneath the arch of the ribs, and the epigastrium is occupied as far as the umbilicus by both lobes of the liver. The region of the right hypochondrium and epigastrium curves forward more strongly. Correspondingly the patient experiences, in the regions mentioned, a sensation of distention, pressure, and tension; occasionally, also, real pain, due to the stretching of the covering of the liver. The organ is readily accessible to palpation, it is felt as a smooth, moderately firm, and uniformly resisting body. If the ductus choledochus is occluded below the entrance of the cystic duct, and the latter is permeable, the gall-bladder will also take part in the dilatation from the retention of bile. It projects beneath the border of the liver as a hemispherical or rounded, elongated swelling, which may be sharply defined by careful percussion. By palpation, also, the gall-bladder is usually readily perceptible as a smooth, tense body, and it is often even visible as a prominent tumor. In some cases the gall-bladder reaches such dimensions that it lies upon the ilium, and simulates an independent, tense cystic tumor, which almost fills the right half of the abdomen. It has often been mistaken, under such circumstances, for a cystic tu-

mor of the ovary, hydronephrosis, and similar conditions, and this may occur so much the more readily, as the gall-bladder possesses, in these cases, an unusually great and free mobility.

The enlargement of the liver usually continues for several months, a halt then occurs, and after this has lasted for some time, a gradually increasing diminution of the organ becomes noticeable, while the gall-bladder remains at its former size, or even projects somewhat more than previously. In the course of the next few months the liver not alone returns to its original normal dimensions, but it often undergoes a still further considerable diminution in size, so that it may now be described as a true atrophy. This is the expression of the gradual disappearance of the secretory parenchyma of the liver and of the diminution of its secretory function. In many cases the atrophy of the organ remains absent, or occurs, at least, within such narrow limits that it escapes observation.

If, after long duration of the occlusion of the bile-duct, the secretory parenchyma of the liver is destroyed in great part, severe nervous symptoms sometimes develop, such as somnolency, disordered consciousness, or complete coma, delirium, convulsions, muscular irritability, singultus, carphologia, paralysis of the muscles, etc.—in fine, a typhoid condition, accompanied by fever, with moderate elevation of temperature, which is disproportionate to the gravity of the entire condition. When these symptoms, which are often known under the not very appropriate term cholæmic intoxication, make their appearance, they forebode, in almost every case, the near approach of the fatal termination. This typhoid condition reminds us, indeed, of certain blood-poisons, but no harmony has been reached in the views concerning its immediate cause, the chemical nature of the poison in question, the manner and situation of its development. With Murchison, we regard it as more probable that the supposed poison is not formed exclusively in the liver, but rather in the blood and in the tissues of the body generally. The liver is not alone the secretory organ of the bile, but also exercises an important influence upon the general nutritive changes, and it especially appears to be the site of formation for urea and uric acid. If the function of the liver is interrupted, it follows that

urea will no longer be formed, while substances like leucin, tyrosin, and other less known bodies, which we are accustomed to regard as stepping-stones between urea and the protein bodies of the organism, will be produced. During this time the materials, which are destined to leave the body as urea and uric acid, accumulate in the blood and may give rise to the symptoms of blood-poisoning described above. The latter will appear so much more markedly when the function of the nervous system, at the same time, suffers considerable diminution.

Diagnosis.

The diagnosis of occlusion of the bile-duct presents no difficulty in itself, as it follows immediately from the presence of retention-icterus which, it goes without saying, must be first determined. A difficulty, however, immediately arises when it is necessary to decide upon what the occlusion of the duct depends and how it has developed, as there are a very large number of diseases attended with retention-jaundice; and on account of the difference in their significance as regards the patient, a correct diagnosis of the pathogeny of the jaundice is of great importance, both with regard to prognosis and treatment.

The first glance shows us, as a rule, whether icterus is present or not. It is hardly conceivable that it should be mistaken for other similar colors of the skin, if we consider that the cases belonging here do not refer to milder grades, but usually to the darkest shades of color—not to a rapidly disappearing jaundice, but to one of long duration—and if we also pay attention, in addition to the color of the skin, to the bile-staining of the urine, and the usually complete discoloration of the fæces. A doubt could only arise in those extremely rare cases in which, despite the complete occlusion of the bile-duct, the icteric color of the skin, conjunctiva, and urine has almost entirely disappeared on account of the continued abolition of the hepatic functions, in case the physician has only seen the patient during this stage. Continued observation of the patient, his own statements, and the complete discoloration of the evacuations from the bowels,

will no longer permit any doubt concerning the fact of occlusion of the bile-duct.

If, however, retention-jaundice has been diagnosed, it remains to determine what causes have given rise to it, or, what amounts to the same thing, to the occlusion of the bile-duct. This demand can only be fulfilled by way of exclusion, and then often only approximately. The chief importance must always be attached to the intensity and duration of the jaundice. In other respects the diagnosis must be based, on the one hand, upon the results of the most careful and thorough examination of the abdomen, especially of the liver and gall-bladder, as well as the adjacent organs, the right lung, stomach, duodenal region, etc., and on the other hand, upon the clinical history, *i.e.*, upon a careful consideration of the circumstances under which the jaundice has developed, upon the course of the present disease, the affections which may have preceded it, etc. In the frequent absence of perceptible anatomo-pathological changes in the domain of the biliary apparatus, a detailed history often furnishes the most valuable data for the diagnosis of the pathogenic factor.

The differential diagnosis is most simple in the new-born. Simple icterus neonatorum rarely continues longer than two weeks after birth. Every severe icterus in the new-born which lasts for a longer period points to an irreparable lesion of the large bile-ducts, as there is no disease of the liver itself at this period of life which is attended with chronic icterus and complete discoloration of the fæces, not even excepting syphilis of the liver. In all probability, however, we must regard this disturbance of the bile-ducts as the so-called absence or fœtal occlusion of the canals, since obstruction of the ductus choledochus in very young children by gall-stones or inspissated bile is of even rarer occurrence, and other anatomical changes are unknown at this age as the cause of permanent retention-icterus. If, therefore, a child becomes jaundiced within the first few days after birth, and the icterus steadily increases, the fæces are entirely discolored and remain so, if hemorrhages occur from the umbilicus or intestines into the skin, etc.; if the previously vigorous and well-nourished child suffers from progressive emaciation, to which vomiting and diarrhœa are often added, and death

only occurs after the lapse of several weeks or months, hardly a doubt can be entertained that we have to deal with congenital impermeability of the large excretory bile-ducts.

Matters are much more complicated in patients at a more advanced period of life. In the first few days of the jaundice, and indeed so long as the latter is not very intense, the circle of diseased processes to which it may possibly be due must be drawn very wide. The domain of the latter becomes daily more restricted, as all affections which produce temporary or less intense jaundice, or in which the flow of bile into the intestine has not entirely ceased, are excluded by this very fact. What then remains corresponds to the "chronic" icterus now under consideration. This, however, may depend upon occlusion of the common excretory bile-duct, the liver being in a normal condition, as also upon certain diseases of the liver, while the common excretory duct remains normal. We must endeavor, as far as possible, to exclude the latter (hepatic affections) in order to fall back upon that category of conditions which we have collected in the section on etiology.

The diseases of the liver, which may be attended with intense chronic jaundice, are: carcinoma and the closely related neoplasms (adenoma, etc.), simple and multilocular echinococcus tumors, idiopathic abscess, syphilis, amyloid degeneration, and, especially, cirrhosis of the liver. We will return to the first two mentioned diseases at a later period, and will content ourselves with the following remarks with regard to the remainder.

Jaundice rarely occurs in idiopathic abscess of the liver, usually remains mild, and is of short duration, corresponding to the rapid course of the abscess. Apart from the fact that these hepatic abscesses occur especially in warm climates, often in consequence of dysentery, the pains in the right hypochondrium and right shoulder connected with them, furthermore, the severe disturbance of the general condition, the febrile symptoms, and, especially, the discovery of a fluctuating tumor connected with the liver itself, hardly render it conceivable that this disease can be mistaken for retention of bile due to occlusion of the ductus choledochus.

With regard to syphilis of the liver, the absolute retention of

bile dependent upon it is only conceivable under the supposition that syphilitic cicatrices and fibrous bands compress the hepatic duct, or its two chief branches near their point of union. This would, therefore, correspond substantially to a perihepatitis, to the consideration of which we shall soon return.

Amyloid degeneration of the liver never, in itself, produces such an intense jaundice as attends closure of the ductus choledochus. When, therefore, an intense and chronic icterus is combined with a demonstrably amyloid enlargement of the liver, we should search for another cause of the occlusion of the duct. The first suspicion would fall upon enlarged and degenerated portal lymphatic glands, which could compress the common excretory duct.

Experience teaches that the differential diagnosis of cirrhosis of the liver (though only the so-called hypertrophic variety) may give rise to the greatest difficulty. In the ordinary form of cirrhosis leading to atrophy of the liver, the jaundice, when not entirely absent, is only present in the milder grades, and the flow of bile into the intestine is never entirely interrupted, the fæces, therefore, not completely colorless. Ascites, on the other hand, is constant; it develops early, and soon attains a high degree. The subcutaneous veins of the abdomen, and the hemorrhoidal veins are markedly dilated, a tumor corresponding to the enlarged gall-bladder cannot be discovered, while the atrophy of the liver reaches a much higher grade than occurs in occlusion of the bile-duct; moreover, whiskey-drinkers are almost the only ones who become affected with this form of cirrhosis. When all these factors are taken together, it is scarcely conceivable that the disease should be mistaken for occlusion of the bile-duct. Matters are different in the rarer hypertrophic form of cirrhosis.[1] In this variety icterus is never absent, continues during the entire course of the disease, extending over several years, and causes, at least at times, a coloration of the skin which is as dark as that found, as a rule, in closure of the ductus choledochus. The jaundice is either mild in the beginning, and gradually

[1] Cf. *Hanot*, Cirrhose hypertrophique du foie. Thèse de Paris, 1876, and also a case lately reported by the same author (Cirrhose hypertr. avec ictère chronique), in Arch. gén. de méd., Jan., 1879, p. 57.

grows more severe, or it appears with great intensity at the onset. It continues until death, but presents considerable variations in severity. The fæces are sometimes discolored, sometimes of a normal appearance. Ascites usually develops very late, and the dilatation of the subcutaneous abdominal veins is absent. The liver is very considerably enlarged, and projects beyond the false ribs by a hand's breadth, or even more. Upon palpation, the liver is felt as a tumor with a smooth surface and of firm resistance. The hepatic region is distinctly prominent, an enlargement of the gall-bladder is not demonstrable. Pains in the region of the liver, developing in paroxysms and irregular attacks of fever, also occur in hypertrophic cirrhosis. The resemblance of this clinical history with that peculiar to occlusion of the ductus choledochus cannot therefore be denied, and, in fact, very acute diagnosticians have declared it almost impossible, in individual cases, to differentiate hypertrophic cirrhosis from the occlusion of the ductus choledochus produced by impacted gall-stones. In the differential diagnosis of these two conditions, special stress must be laid upon the following points. The enlargement of the liver does not attain such a high grade in closure of the gall-duct as in hypertrophic cirrhosis. The enlargement of the gall-bladder, which is present and also demonstrable in the former, in the majority of cases, is absent in the latter. It is especially noteworthy also that the pains, which occasionally develop in the region of the liver in hypertrophic cirrhosis, do not present the peculiarities which are usually so characteristic of the colic produced by impacted gall-stones. But we must also not forget that the attacks of colic in the affection due to hepatic calculi are not always sharply defined, especially when the calculi have closed the gall-duct for months, and have acted as the exciting cause of inflammatory changes in the latter and perhaps also in the liver.

We now come to the differential diagnosis of those conditions which may produce closure of the common excretory duct of the bile, and which have been mentioned above.

As far as regards occlusion of the ductus choledochus by impacted gall-stones, we do not now refer to ordinary cases of temporary impaction, but to those exceptional instances in which

a large gall-stone always remains in the duct and causes permanent jaundice. We may accept this as the cause of the occlusion when the history shows that the patient has formerly suffered from paroxysmal pains in the hepatic region with jaundice of short duration, or, at least, that such attacks of pain have preceded the present continuous icterus; that gall-stones were found, at some former time, in the stools of the patient, or that some symptoms of cholelithiasis had been observed in him. The liver will be found of nearly normal size, or, at the most, only moderately enlarged; the gall-bladder, as a rule, however, projects beneath the border of the liver as a round, fluctuating tumor. Pressure upon this tumor causes painful sensations. As the impacted calculus would probably always escape immediate observation by palpation, the fact that no firm spot or tumor can be discovered in the region of the liver by which the icterus can be explained can be readily made to agree with the diagnosis of occlusion by gall-stones. Ascites is absent or only develops toward the end of the disease. Exceptionally, it has been observed from the beginning in combination with icterus, when the calculus, which obstructs the ductus choledochus, also exercises, at the same time, a serious pressure upon the adjacent trunk of the portal vein. The general condition of nutrition in gall-stone occlusion remains good for a long time, and emaciation and marasmus only become noticeable at a late period. Febrile symptoms of an irregular character, which are caused by inflammatory processes in the bile-ducts, rather favor the diagnosis of calculi, because impacted gall-stones usually produce inflammations of the gall-ducts. We must also bear in mind the circumstances (sedentary habits, etc.), which influence the occurrence of cholelithiasis. Especial attention must be paid to the age of the patient, as gall-stones are very rare before the thirtieth year.

The closure of the bile-duct by parasites next merits consideration. On account of its position with relation to the transverse fissure of the liver and to the bile-ducts which there make their exit, the ordinary hydatid tumor cannot readily cause such an intense and protracted jaundice as is characteristic of occlusion of the ductus choledochus; and, if it did occur, the sac could with difficulty escape the observation of the physician. But the view

that, in a case in which occlusion of the ductus choledochus is demonstrated, this occlusion is produced by echinococcus vesicles, which have passed from a ruptured hepatic sac into the gall-ducts, may be accepted under the following circumstances: The physical signs of an hydatid tumor of the liver must have been present before the accident in question, and the tumor referred to must have become smaller with the occurrence of the occlusion of the bile-duct. The passage of echinococcus vesicles into the gall-ducts and their progress in the latter are attended by severe paroxysms of pain, chills, vomiting, in short, by all the symptoms which are caused by the passage of gall-stones through the canals, and which are known under the term hepatic colic. No biliary concretions, however, but echinococci, are found in the stools, thus at the same time furnishing the most positive data concerning the nature of the attacks of colic. The closure of the ductus choledochus produced by echinococcus vesicles also differs from that due to gall-stones, in the fact that continued fever with high temperatures is present in the former, because the bile which enters the ruptured sac causes it to become inflamed. If no bile enters the sac, the continued fever will remain absent. The extremely rare cases in which an echinococcus sac appears to have developed primarily in the gall-ducts are entirely incapable of diagnosis.

The multilocular echinococcus tumor of the liver is often differentiated with very great difficulty, especially in the earlier stages of the disease, from simple occlusion of the ductus choledochus. In the former hepatic affection the jaundice is due to closure of the hepatic duct, and the enlargement of the gall-bladder, which develops, as a rule, in closure of the ductus choledochus, will not be observed. However, the differentiation of the two conditions mentioned will only be brought into question in those localities in which the multilocular echinococcus tumor occurs, viz., in the southwestern part of Germany and in Switzerland. As soon as a tumor of the liver is demonstrable the difficulty in diagnosis diminishes. This tumor of the multilocular echinococcus is usually situated in the right lobe; is at first very firm, uneven, and nodular; may attain very considerable dimensions, and, in its further course, may be trans-

formed into a fluctuating tumor by ulcerative degeneration at its centre. In multilocular echinococcus the spleen is enlarged in the majority of cases, a symptom which is not present in closure of the ductus choledochus; ascites is more rarely present, or only develops in the later stages. With regard to the ascites, therefore, as well as the jaundice and the general marasmus, both abnormal conditions present a similar behavior. In a word, the differentiation from one another remains impossible, or is extremely doubtful, so long as the tumor present in the liver escapes direct observation.

The diagnosis, that a long-continued occlusion of the bile-ducts is caused by liver-flukes or round-worms, is also a very dubious matter, since, however frequently the parasites mentioned, at least the round-worms, are found in the gall-ducts, complete retention of bile continuing for months is rarely produced by them. That the latter is caused by liver-flukes can only be accepted with a certain degree of probability in those instances in which one of these worms is discharged with the vomit or in the stools. In other respects the liver-flukes substantially give rise to the symptomatology of chronic cholangoitis. Round-worms, by their penetration into the bile-ducts, may give rise to the symptoms of jaundice, biliary colic with acute attacks of pain, vomiting, etc. Sudden death sometimes occurs (in small children) in violent convulsions. In individuals who have previously passed round-worms in the stools or in the vomit, the latter may be suspected as the cause of the occlusion of the bile-duct as soon as they are affected by jaundice. This diagnosis is probably correct if no more plausible cause of the jaundice can be found, as, for instance, an indigestion, a violent cold—in short, the usual causes of so-called catarrhal icterus. Furthermore, if it relates to individuals during childhood, in whom round-worms occur with special frequency, and especially when, after the administration of a laxative or anthelmintic, the retention of bile appears to disappear promptly with the discharge of round-worms. However, the coincidence of the discharge of the worms with the disappearance of the jaundice is not a sufficient proof that these worms have occluded the bile-ducts; a catarrhal icterus may still have existed without the entrance of worms into the gall-ducts.

That the occlusion of the biliary excretory duct is due to fibroid thickening of its walls or to continuous inflammatory swelling of its mucous membrane in the narrow pars duodenalis —*i.e.*, to anatomical lesions, which belong to chronic catarrhal or phlegmonous cholangoitis—may be diagnosed (though only presumably) when no more plausible mechanical cause of the occlusion can be discovered, when the course of the disease in its first stages has corresponded to that of so-called simple or catarrhal icterus, and when, finally, one of the common causes of cholangoitis has demonstrably preceded it. Among these factors must be mentioned, in addition to spoiled stomach, cold and similar causes of gastroduodenal catarrh, especially also the passage of gall-stones and other foreign bodies through the bile-ducts, as all these foreign bodies, even though they have left the duct itself, may be followed by more or less deep-seated inflammations of those portions of the canal through which they have passed, with all their serious consequences.

The occlusion of the biliary excretory duct by fibrous bands, which have developed in the course of perihepatitis, exactly like the just mentioned occlusion following chronic cholangoitis, is recognized with very great difficulty in the living subject. This diagnosis is only allowable under the following circumstances: It must follow from the clinical history that one of the common causes of perihepatitis has been present in the patient in question as, for instance, a round gastric ulcer, inflammation of the right pleura, general peritonitis, certain diseases of the liver, and especially, also, constitutional syphilis. We must also be able to deduce from the history, as well as the present condition of the patient, that the perihepatitis really exists, and it is especially true that sharp pains, a feeling of tension and pressure in the right hypochondrium with more or less marked febrile symptoms must be present. If, in addition to these symptoms, the signs of chronic atrophy of the liver and of occlusion of the portal vein, viz., ascites, intestinal hemorrhage, diarrhœa, dilatation of the subcutaneous abdominal veins, etc., become noticeable, and if there is nothing present which might be attributed to a previously existing hepatic colic or to a carcinomatous affection, we possess all the data which can be adduced in favor

of the occlusion of the bile-ducts by the products or remains of a perihepatitis.

With regard to stenosis of the excretory duct by retracting cicatrices of ulcers in the course of the duct itself, we must take into consideration, in the diagnosis of this condition, that such ulcers occur, as a rule, from gall-stones, more rarely in consequence of typhoid fever and similar severe infectious diseases, and only in extremely rare cases without any known cause. The differential characteristics of this condition may be mentioned as follows: In many cases the clinical history indicates that attacks of gall-stone colic have been previously present. In all those cases in which permanent icterus without pain has developed after the symptoms of cholelithiasis, the suspicion arises that either a gall-stone has been firmly and permanently impacted or that an organic stenosis or occlusion of the duct from the cicatrix of an ulcer has occurred. If the ulcer of the gall-duct has developed independently of calculi, the diagnosis of occlusion by the retraction of the ulcer of the cicatrix will, as a rule, remain doubtful, because such ulcers do not always present characteristic symptoms. As ulceration of the gall-ducts is sometimes combined with abscess formation in the liver, some ground for the diagnosis of cicatricial stenosis would perhaps be afforded if it could be determined that the signs of hepatic abscess, viz., fever with frequent chilly sensations or chills, great and irregular changes of temperature, accompanied by pains or at least by disagreeable sensations in the region of the liver, had been previously present.

Closure of the ductus choledochus by a cicatrized duodenal ulcer also presents the greatest difficulties in diagnosis. We must suspect this form of occlusion if the signs of a perforating duodenal ulcer have been observed in the patient before the development of the jaundice, as, for instance, pains in the right hypochondrium, which only appear a few hours after meals, at a time, therefore, in which the contents of the stomach pass into the duodenum, and furthermore, suddenly developing attacks of profuse hæmatemesis with bloody stools, followed by extreme anæmia and exhaustion, etc. It is, however, well known that these symptoms are often absent in perforating duodenal ulcers,

that they may remain latent and not reveal their existence until the fatal perforation has occurred. So long, therefore, as the circumstances attending a concrete case do not point to any other definite cause of the occlusion of the ductus choledochus, the possibility may still be allowed that the latter is produced by a cicatrizing duodenal ulcer, even in the absence of positive proofs of the existence of such a lesion. As duodenal ulcers, which are situated in the region of the porus biliarius, may give rise to attacks of pain in the abdomen, followed by jaundice, we must, in consideration of these facts, regard it as impossible to differentiate occlusion of the bile-duct by the cicatrix of a duodenal ulcer from that produced by an impacted gall-stone.

We must think of occlusion of the ducts within or without the liver by cancerous and cancroid neoplasms, which start from the liver or from the very walls of the bile-ducts, compress the canals, and infiltrate their walls or distend their lumen, when cancerous nodules are either directly demonstrable by palpation in the region of the liver, or when a cancer has at least been shown to be present in other organs (especially the stomach, intestines, peritoneum, etc.) which may possibly have given rise to the formation of secondary nodules in the liver; when, furthermore, the symptoms of cancerous cachexia are present and when the icterus first shows itself after the signs of a malignant tumor have preceded, and when finally no more probable cause of the biliary retention can be discovered.

With reference to occlusion of the bile-duct by cancer of the duodenum (and also of the head of the pancreas), which displaces the mouth of the duct or grows into its lumen, the diagnosis must be based on the following points: The patient usually complains for several weeks before the occurrence of jaundice of more or less severe pains (at times of a lancinating character) in the region of the duodenum. The pain also continues after the development of jaundice, and generally undergoes an exacerbation a few hours after meals. Nausea and tendency to emesis are present in the majority of cases, especially after eating. Hæmatemesis and bloody stools may also occur occasionally, particularly when ulcerative degeneration of the duodenal cancer has set in. In only a few cases can a hard, tense tumor be more

or less distinctly felt upon careful palpation through the abdominal walls. The jaundice continually increases in severity until death. This occurs, in the majority of cases, in about four or five months after the development of jaundice. This circumstance is important, as the mere fact that intense jaundice has continued more than six months, indicates, as a rule, that the closure of the ductus choledochus has not been caused by a cancerous tumor. Even this rule, however, is not without exceptions. Moreover, progressive emaciation and weakness, as well as the other signs of the cancerous cachexia, are noticeable both before as well as after the appearance of jaundice. The demonstration of cancer in other parts of the body, or the fact that carcinoma has often appeared in the patient's family, will be a further support of the assumption of cancerous occlusion.

The diagnosis of occlusion of the biliary excretory duct by enlarged lymphatic glands (cancerous, amyloid, lymphosarcomatous, tubercular, or cheesy) in the transverse fissure of the liver must be made to depend upon the proof of the existence of a cancerous affection of the liver, stomach, etc., of waxy liver, general tuberculosis, lymphosarcomatous tumors in the neighborhood of the liver, etc., and furthermore, upon the ascites which is usually present at the same time, since the glandular tumors generally exercise pressure upon the portal vein as well as upon the bile-duct. Under certain circumstances the enlarged portal glands will be accessible to palpation, or examination of the region of the liver will at least reveal a tumor, concerning which we can assume that it may have caused the secondary enlargement of the portal glands.

Cancer of the stomach should be thought of as the cause of occlusion of the ductus choledochus, when the jaundice is preceded and accompanied by the ordinary symptoms of cancer of the pylorus, especially by pains and vomiting after meals, by the vomiting of "coffee-grounds" masses, and by rapid emaciation, when, furthermore, a tumor can be discovered whose position corresponds to the region of the pylorus and when a high degree of gastric dilatation is present.

The occlusion of the bile-duct, which is produced by tumors in the head of the pancreas, presents symptoms similar to those

already mentioned of occlusion by duodenal cancers. In cases of pancreatic cancer, pains will develop, which, from their position may be referred to the pancreas, and nausea and tendency to vomiting will also be present. A hard tumor, which corresponds with the situation of the pains, jaundice continuing until death, rapid emaciation, and the other signs of cancerous cachexia, and especially the evacuation of large masses of fat in the stools, which is sometimes observed, confirm the diagnosis. Other tumors of the head of the pancreas occur too rarely as causes of occlusion of the bile-duct to permit the question to arise of a differential diagnosis which will possess any certainty.

With regard to occlusion by retroperitoneal and omental tumors (chiefly of a carcinomatous nature) such growths will, indeed, not escape observation when they have become so large as to compress the bile-duct. The diagnostic difficulty consists rather in determining the starting-point of such tumors. Especially is it sometimes difficult to differentiate an omental growth in the neighborhood of the liver from a tumor of the liver itself. In this matter we must rely upon the statements of the patient and upon the observation of the manner in which the tumor grows. Practically, however, the subject does not possess any great importance, as we are impotent against all these conditions.

Occlusion of the biliary excretory duct by an aneurism is one of the rarest problems for differential diagnosis. Although aneurisms of the hepatic artery, which must be chiefly considered on account of the position of this vessel with regard to the gall-duct, are very rare, they nevertheless appear to be pretty well defined during life. According to Frerichs, who has collected four of these cases, the aneurism may be recognized as belonging to the hepatic artery: by the symptoms of imperfect duodenal digestion, by pains in the duodenum and its neighborhood, which occur two to three hours after meals, by attacks of severe neuralgic pains in the hepatic region, which simulate hepatic colic, and are undoubtedly due to the pressure exercised by the aneurism upon the nerve-plexus of the liver, by continuous jaundice on account of the compression of the bile-duct, by attacks of hæmatemesis with bloody stools (rupture of the aneurismal sac into the biliary

passages or directly into the duodenum), and, consequently, extreme anæmia; finally, by a tumor in the right hypochondrium which may displace the liver upward. In Stokes's case, pulsation of the aneurismal tumor was absent. With regard to Gairdner's remarkable case—in which jaundice was produced by an aneurism of the superior mesenteric artery which had opened, twenty-two months before death, into the duodenum, and had given rise to repeated severe hæmatemesis with symptoms precisely similar to those of perforating gastric ulcer—this observer remarks that the combination of jaundice with the signs of disordered duodenal digestion (cardialgia, pain and vomiting some time after eating) should always awaken suspicion of a tumor which presses upon the gall-duct and pancreas at their duodenal end; and, also, that the coexistence of these symptoms with fixed pain or pressure in the epigastrium, with a feeling of pulsation in this region and with hæmatemesis, very probably points toward an aneurismal tumor, especially in the absence of any positive proofs of any other more frequently observed form of occlusion of the ductus choledochus.

Finally, the diagnosis of biliary retention which is produced by large tumors of the ovaries and uterus reaching to the liver, or by large tumors of the right kidney, presents no difficulties. This is also true of the jaundice due to the pressure of an accumulation of fæces, or the uterus in the last stages of pregnancy. The rapid disappearance of jaundice, in the first case, after the administration of cathartics, and the appearance of jaundice in the advanced stages of pregnancy and its disappearance soon after the occurrence of delivery, allow no doubt to arise with regard to the connection of the symptoms in question.

Course, Terminations, Duration.

In occlusion of the biliary excretory duct we have to deal with conditions, the large majority of which not only develop gradually on account of the nature of their causes, but also, in general, pursue a chronic course. There is, indeed, no dearth of exceptions to this rule, inasmuch as even a complete and permanent occlusion may suddenly develop as, for instance, from

impacted gall-stones, echinococcus vesicles, etc., while its course may be shortened to less than the duration of many so-called acute diseases by the occurrence of the fatal termination within a few weeks or even days.

Occlusion of the biliary excretory duct may have a twofold termination in recovery or in death. Relatively few cases undergo recovery, viz., those in which a removal of the causes is possible, as, for example, in closure of the ductus choledochus by foreign bodies. When, however, long-continued occlusion of the gall-duct has taken place, the concrete circumstances are notoriously of such a character that, although the above termination is possible, the removal of the occlusion does not practically occur. It may also be included among recoveries, when the consequences of the occlusion are relieved by any accidental circumstance, although the stenosis itself still continues. When, for instance, a gall-stone, which has for a long time been impacted in the ductus choledochus, has led to all those changes which we have learned to recognize as the consequence of occlusion of the duct, and if a fistulous communication of the gall-bladder with the duodenum occurs by perforation, by which the retained contents of the biliary canals find a free passage into the upper portion of the intestines, there is nothing to oppose the removal of all the evil consequences of closure of the ductus choledochus, although the latter continues unchanged.

The rule is, therefore, that closure of the canal leads to death, usually from cholæmia (in its broadest sense). In rarer cases it is not the retention of bile, or at least not this alone and chiefly, which is followed by death, but rather the causes of the occlusion themselves, even when they do not lead to retention of bile and jaundice as, for instance, in cancer of the ductus choledochus. That the cause of death may also reside in other, more accidental, or at least not constant sequences of the occlusion as, for instance, in a suppurative cholangitis, is as evident as the possibility of a fatal termination in consequence of the most varied intercurrent accidents.

With regard to the duration of the disease, the question as to the length of time during which complete closure of the ductus choledochus, with all its consequences, can be tolerated by the

organism, has been discussed with great interest.[1] Experience teaches us the following: small children, with congenital absence or closure of the ductus choledochus, die from the mere consequences of the occlusion, if no other disorders co-operate, and in the majority of cases within a few (three to four) weeks. In individual cases, however, the children attained the age of several months. The longest duration is reported by Nunneley (Path. Trans. Vol. XXIII. 1872, p. 152). The child observed by him reached the age of six months and twenty-one days.

The conditions are less simple in adults. In the first place, the duration of the disease is different in them, according as the retention of bile and its sequences alone come in question, or whether the disorder which has given rise to the occlusion of the ductus choledochus, also exercises a deleterious influence upon the organism. The duration of the retention of bile is markedly shorter when cancerous and similar tumors have produced the occlusion.

In cases in which the pathogenetic factor is immaterial to the organism, as, for instance, in adhesive cholangitis or simple closure by gall-stones, everything depends upon how long the body can tolerate complete retention of bile. But various factors act together, whose share we must take into consideration, viz., 1, the absence of bile for the purposes of digestion; 2, the saturation of the blood and nutritive fluids of the body by biliary constituents; 3, the diminution and final abolition of the secretory function of the liver, which occasionally occurs; and 4, the more or less effective action of the kidneys in regard to the elimination of biliary constituents from the blood. The duration of the disease varies within very broad limits, according to the preponderance of one or the other factor. The significance of each of the

[1] Cf. *Hertz*, Berl. klin. Wochenschr. 1877. No. 6 and 7. In a man æt. seventy-one years, the stools had been completely discolored for two and three-quarter years, although icterus only occurred periodically in eight attacks, which were combined with fever; it was entirely absent in the intervals. No symptoms on the part of the liver; general emaciation and weakness. The appetite was tolerably fair. The autopsy showed occlusion of the ductus choledochus by a gall-stone. As no jaundice occurred, with the exception of the short attacks, despite the absence of any escape of bile, Hertz supposes that the secretion of bile was abolished. Nothing noticeable was found in the liver.

factors just mentioned cannot, as is readily understood, be separately ascertained, but so much is certain, that adults can, in general, tolerate retention of bile and its consequences surprisingly long, and, in individual cases, well and readily. Even the possibility of recovery is not excluded after the retention of bile has lasted for years. In this respect experience teaches the following: the diminution in the size of the liver is found to begin, on the average, after the biliary retention has lasted three to four months, and in eight to twelve months the ominous hemorrhages from the intestines, etc., appear, as well as the severe cerebral symptoms, which we are accustomed to explain by the rapid degeneration of the liver-cells. However, there are numerous exceptions to this. The example of two and three-quarter years' duration by Hertz, previously referred to, is not the most extreme. Budd mentions a case of jaundice, from closure of the ductus choledochus, which continued nearly four years, during which the patient was in a satisfactory condition, and the muscles remained vigorous. Murchison furnishes a case of complete occlusion by gall-stones, with jaundice and discoloration of the fæces, in which recovery set in after the lapse of six years. And Barth and E. Besnier[1] describe a child (age ?) with complete retention of bile and greenish color of skin, enormous enlargement of the liver and spleen, in whom all the functions were properly performed, who had a good appetite, digested well, had no pain or fever, slept well, experienced no local distress, worked without any mental strain, remained physically strong, was in good humor, and in whom recovery occurred after the lapse of six years under the continued administration of small doses of calomel. Similar cases are not extremely rare in literature.

Prognosis.

The prognosis depends, in the first place, upon the nature of the cause producing the occlusion, and in the second place, upon the manner in which the organism tolerates the retention of bile. If the pathogenetic element of the disease is irreparable, the

[1] Dictionnaire encyclop. des sc. méd. by *Dechambre*. Vol. IX., p. 348.

prognosis must be regarded as fatal. As a rule, we must assume such a non-removable cause of the occlusion when the jaundice continues a long time, although there are numerous exceptions.

The intensity of the yellow color of the skin is not of very great importance with regard to prognosis, and it may appear slight in the most grave conditions. Commonly, however, the deep olive-green or bronze-like color of the integument, as well as the permanence of the icterus, are of bad omen. A change in the color of the skin allows us to believe that the obstruction to the escape of bile is not complete and incurable, but in this respect more accurate information is furnished by the, at least, partial return of color to the fæces. Furthermore, the pruritus is also an aggravating circumstance when it attains any considerable intensity; the pain, irritability, and insomnia hasten the decay of the organism. The development of hemorrhages from the mucous membrane of the intestines, etc., as well as the severe nervous symptoms of so-called cholæmic poisoning, herald the near approach of the fatal termination.

The fact that recovery is sometimes found to occur, even after the retention of bile has lasted for months and years, must be a warning to the physician to be correspondingly guarded with regard to the prognosis. In the first months of the disease the physician should be extremely cautious in giving an opinion concerning the possible termination, especially when the cause of the occlusion has not been positively settled.

Treatment.

It is not within the power of the physician to remove the causes of the occlusion. Treatment can therefore only have for its object to relieve the most annoying symptoms, and those factors which aggravate the condition of the patient, to aid the separation of the biliary constituents from the blood, and to maintain the nutrition and strength of the patient as long as possible.

The greatest attention must be paid, above all things, to the regulation of the diet and the evacuation of the bowels. The patient should be fed upon milk, eggs, lean meat; articles

which are digested with difficulty, and those which are fatty, as well as strong alcoholic drinks, must be forbidden. Very abundant meals, to which some patients of this kind have a tendency, must be avoided. The various stomachics, the bitter vegetable extracts, etc., may be resorted to in order to aid the appetite and digestion. The tendency to constipation should be counteracted by the methodical use of Carlsbad salts and other saline remedies, and the corresponding mineral-waters. In case of necessity, drastics cannot be dispensed with. Against flatulence, which is due to imperfect changes in the intestinal contents on account of the absence of bile in the intestines, are recommended the use of purified animal gall (from the ox, etc.) in doses of 20–40 ctgr., two hours after meals, in pills or capsules, and, furthermore, creosote, turpentine, and carbolic acid, as substitutes for the antiseptic action of the bile. Cholate of soda (50–60 ctgr.) in peppermint-water, the alkaline carbonates and mineral-waters, perhaps in combination with extract. taraxaci, gentian, preparations of quinine, often possess a good effect, not alone upon the flatulence, but upon the digestive disturbances of all kinds.

Against the icterus as such (especially in the first stage of the disease, in which a hope of its disappearance is still held) we may make use of all those remedies, which have been advised for one reason or another, and have been found, empirically, to be of value. This is especially true of the cholagogues proper, among which the alkalies and alkaline mineral-waters (Ems, Vichy, etc.) probably take the first rank. In the later stages it is better to avoid the use of this group of remedies.

The annoying pruritus of the skin proves extremely obstinate under treatment. Cold washing, lukewarm baths with subsequent shower-douche, fatty and irritating inunctions of the skin, have the best effects upon it. The bicarbonate of soda taken internally, furthermore, acetic acid baths (½ litre acetic acid to 25 litres water), friction of the skin with a mixture of one part chloroform to five parts glycerine (Murchison), corrosive sublimate washes, and other remedies, sometimes prove useful. Often nothing remains but the employment of morphine to procure sleep when the pruritus is intractable.

To obtain prompt elimination of the biliary constituents from

the economy, it appears advisable to take large quantities of water into the body, in order to produce a more rapid change of fluids, and, in a certain sense, to saponify and wash these substances out of the system. This result can be still further secured by stimulating the action of the kidneys, skin, and intestines by means of suitable diuretics, diaphoretics, and drastics.

Apart from dietetic measures, tonics such as quinine, preparations of iron, and similar remedies, may be employed against the gradually developing anæmia and the loss of energy. All medicinal treatment is often useless in incurable closure of the gall-duct.

Dilatation of the Gall-Bladder.

(Simple Dilatation, Dropsy, and Empyema of the Gall-Bladder.)

J. L. Petit, Remarques sur les tumeurs formées par la bile retenue dans la vésicule du fiel et qu'on a souvent prises pour d'abscès du foie. Mémoires de l'acad. roy. de chirurgie, T. I., 1743, p. 168.—*Moraud*, Observat. sur des tumeurs à la vésicule du fiel. Ibid., T. III.—*Morgagni*, De sedib. et caus. morb. 1762. Epist. XXXVII., art. 13.—*Cruveilhier*, Anatom.-patholog. Atlas, 29 livr., pl. 4.—*Albers*, Atlas d. pathol. Anat. IV., Taf. 36. Erläuterungen dazu. IV., I. Abth., p. 47.—*Bamberger*, Krankhtn. d. chylopoët. Systems (Virchow's Handb. d. Path. VI., I.). 1855, p. 634.—*Pepper*, Causes of diseased gall-bladder, etc. Amer. Journ. of Med. Sciences. Jan., 1857.—*Frerichs*, Klinik d. Leber Krankhtn. II. 1861, p. 441–447.—*Erdman*, Ein Fall von Colossalem Hydrops vesic.-felleae. Virch. Arch. XLIII., p. 289.—*Ch. Murchison*, Clinical Lectures on Diseases of the Liver. 2d ed. 1877, p. 523.—*Marion Sims*, Remarks on Cholecystotomy in Dropsy of the Gall-Bladder. Brit. Med. Journ., June 8, 1878, p. 811.—*Kocher*, Mannskopfgrosses Empyem der Gallenblase. Heilung durch Incision. Correspondenzbl. f. schweiz. Aerzte. VIII. Jahrg., 1878, No. 19.—*George Brown*, On the Treatment of Dropsy of the Gall-Bladder by Operation, etc. Brit. Med. Journ., Dec 21, 1878, p. 916.—*Keen*, A Case of Cholecystotomy, etc. Amer. Journ. of Med. Sciences, Jan., 1879.—*Lawson Tait*, Cholecystotomy, etc. The Lancet, Nov. 15, 1879, p. 730.

Those cases are termed simple dilatation in which the gall-bladder is distended by an excessive accumulation of ordinary bile into a thin-walled sac of sometimes very considerable dimensions, although no other anatomo-pathological changes of any kind have occurred in the organ. In dropsy of the gall-bladder

(if we employ this term in its strictest sense), no ingress or egress of bile occurs from the organ; the cystic duct, or the neck of the bladder, is permanently closed, and the gall-bladder, which is isolated from the other biliary passages, represents a closed, cyst-like sac, with watery contents which are free from bile. Finally, the inflammatory swelling or empyema of the gall-bladder depends upon the accumulation of purulent products of inflammation, and the organ presents itself as a sac which contains either pure pus, or pus mixed with bile in large quantities.

The diseased conditions mentioned are, therefore, not by any means identical either in their character or their anatomical relations, but they present to the physician one common and important feature, viz., the increase in the size of the gall-bladder. Moreover, there are so many gradations and variations from one condition to the other, that an attempt at a strict separation of the individual varieties promises little success. The various forms of dilatation of the gall-bladder were occasionally grouped by the older authors under the indifferent title of cholecystoncus (tumor of the gall-bladder). Strictly speaking, however, this term also includes cancer of the gall-bladder as well as those cases in which calculi have accumulated in the organ to such an extent that the latter presents itself as a distinct hard and sometimes nodular tumor. The term tumeur biliaire (biliary tumor), which is frequently employed in France, originally had a purely symptomatic meaning, inasmuch as it applied to every enlargement perceptible externally which contained bile. J. L. Petit had already referred to the fact that such a tumeur biliaire could be an hepatic abscess as well as an inflammation of the gall-bladder. At the present time the term is chiefly applied to the inflammatory tumor, or to empyema of the gall-bladder, and, less often, the same expression is used for the other enlargements of the gall-bladder due to the accumulation of bile.

Etiology.

The cause of simple dilatation of the gall-bladder consists, as a rule, of closure of the ductus choledochus, whether this is temporary—produced by catarrhal swelling of its mucous membrane

or by wandering gall-stones—or permanent, as in obliteration of the canal by impacted gall-stones, cancer, etc. Under such circumstances the gall-bladder may become transformed by the bile, which accumulates in it, into a large, thin-walled, fluctuating sac of sometimes monstrous proportions. It is well known, however, that the gall-bladder very rarely attains such an excessive size under these circumstances, and in temporary closure of the ductus choledochus especially it usually remains within very moderate limits. If the occlusion is permanent, the appearances previously discussed will develop in the biliary passages (*vide* p. 595).

It has been observed in a few cases that gall-stones, which remain in the neck of the gall-bladder or in the ductus cysticus, to a certain extent play the part of a valve in relation to the bile, inasmuch as they permit its passage into the gall-bladder, but, on the other hand, render its escape impossible. The simple dilatation of the gall-bladder which occurs in this manner will be diagnosed with very great difficulty, because jaundice is naturally absent in such cases and the stools remain colored.

In rare cases simple dilatation of the gall-bladder also appears to occur without closure of the ductus choledochus, and depends upon paralysis of its walls, *i.e.*, of its muscular coat, without the concurrence of symptoms of cholecystitis, of which the paralysis might be regarded as a sequence. This condition has its analogue in the dilatation of the paralyzed bladder by retention of urine.

While the etiology just referred to is not entirely undisputed, it is, on the other hand, undoubted that the excessive accumulation of bile and the dilatation of the gall-bladder are occasionally of traumatic origin. Even then, however, the immediate anatomical cause of the disorder—whether paralysis of the wall of the gall-bladder or inflammatory swelling of the mucous membrane of the cystic duct, etc.—cannot be positively determined. Jacob mentions a case of rapidly-increasing dilatation of the gall-bladder in an Irishman, æt. twenty-two years, who had received an injury of the right side by a fall into a ditch seven feet deep, and, in addition, became affected with pneumonia. We will

recur, at a later period, to this case, which is also interesting in its therapeutic relations.

Dropsy of the gall-bladder requires, as a pathogenetic premise, the permanent impermeability of the cystic duct in some portion of its course. As a rule, the impermeability is caused by gall-stones, which have become impacted in the neck of the gall-bladder or in the duct itself. More rarely it is due to obliteration of the duct in consequence of adhesive cholangitis, which, again, is usually dependent on the irritation of a calculus. As soon as the flow of bile to and from the gall-bladder has entirely ceased, the hitherto purely biliary contents of the gall-bladder, which is probably always in a condition of chronic inflammation, slowly undergo a radical change; the biliary constituents and mucus are gradually absorbed, and the organ is filled instead with serum, which transudes from the blood-vessels of the walls of the organ. If the chronic inflammation of the wall of the gall-bladder continues and even becomes more intense, the tumor caused by the organ can increase in size with relative rapidity, and its dilatation may attain a surprisingly high grade. If, however, the inflammatory condition of the walls soon subsides, the water-holding sac of the gall-bladder remains indeed enlarged, but does not exceed moderate dimensions. It then usually remains stationary for the remainder of life.

The inflammatory enlargement of the gall-bladder usually does not attain any very considerable dimensions as long as the cystic duct and ductus choledochus remain open, and therefore the escape of pus may occur into the intestinal canal. Affairs assume a different aspect, however, when the cystic duct is closed by gall-stones, etc. The pus secreted upon the surface of the mucous membrane must then accumulate in the cavity of the gall-bladder, and its amount may become so large, when compared with the bile which remains, that the large sac appears to contain purely purulent contents, and constitutes empyema or abscess of the organ. The most common cause of purulent cystitis in closure of the cystic duct consists in the presence of gall-stones. An inflammation of the gall-bladder with profuse formation of pus may also result from excessive distention of the organ by an accumulation of bile in consequence of closure

of the ductus choledochus. In such an ensemble of circumstances the dilatation of the gall-bladder usually increases rapidly in proportions, and sometimes attains an excessive size. The contents of the organ will then naturally form a mixture of pus and bile.

Pathological Anatomy.

In simple dilatation no further anatomo-pathological changes can be observed in the gall-bladder beyond its increase in size. Its wall is correspondingly attenuated, and the mucous membrane smoother. The gall-bladder is sometimes firmly, sometimes loosely, adherent to the liver; it presents, as a rule, no adhesions to surrounding parts, and the sac is therefore movable. The cystic duct is also usually dilated and permeable. The size to which the gall-bladder dilates varies extraordinarily, and in some cases is truly monstrous. It forms a pyriform tumor, the fundus of which sometimes extends to the ileum. Babington [1] reports a case in which the gall-bladder contained three wash-basinfuls of bile, and Copland (ibid.) mentions another in which the organ contained eight pints of bile, and was so large that it pushed the false ribs forward on both sides of the body. On an average, however, the simple dilated gall-bladder will hardly contain more than ½–1 litre. With regard to the constitution of its contents, it approaches that of pure bile so much the more, the less the dilatation and the shorter the period of its development. If a long time has passed and the dilatation of the biliary passages has attained a very high grade, the contents will become paler and more fluid; in individual cases, in which the secretion of bile has been diminished for a long time, the specific constituents will be entirely absent, and instead of the bile a watery or thin, mucous, almost colorless or very pale green fluid appears, which contains no albumen. Under such circumstances we are justified in calling this condition dropsy of the biliary passages.

Sacculated dropsy of the gall-bladder presents itself in its developed and stationary condition as a closed, cyst-like tumor of a pear shape, which is filled with colorless serum. In addi-

[1] Quoted by *Murchison*, l. c., p. 523.

tion, gall-stones (numerous, small, faceted concretions) may also be present in the organ. The wall of the latter is thin, and, after long continuance of the dropsy, fibro-cartilaginous plates or bony and calcareous layers occasionally appear upon the sac and in its walls. The inner surface of the mucous membrane no longer presents the characteristics of such a structure, but is perfectly smooth, shining—has, indeed, adopted all the peculiarities of a serous membrane and appears covered with a delicate layer of pavement epithelium instead of the cylindrical epithelium which is normally present. The few mucous glands of the gall-bladder and its muscular coat have undergone atrophy or have entirely disappeared. Adhesions of the dropsical gall-bladder with the adjacent organs are, as a rule, absent. The duct of the gall-bladder is found closed. Such water-holding sacs rarely exceed the size of a man's fist. If, however, a slow inflammatory process becomes established in it, its size increases very considerably, and in individual cases even to an inordinate extent. It has been observed several times that dropsy of the gall-bladder extended to the ileum, that it even filled the entire abdomen, so as to present the picture of free ascites. Erdmann[1] reports a case in which the almost incredible quantity of sixty to eighty pounds of fluid are said to have been removed at one time by puncture of the gall-bladder.

Empyema of the gall-bladder appears as a tensely filled pyriform, oval, or rounded sac, which is about as long as the hand, and whose thickness may correspond to the width of the hand. It has, however, also been found to attain the dimensions of a man's head (Kocher). The sac is sometimes free, sometimes loosely joined by inflammatory adhesions to the abdominal walls, the omentum, and intestines, with which it is in contact, or even adherent to them by firm fibrous adhesions. Its walls are sometimes thickened and flesh-like from the inflammation, sometimes, however, attenuated, at least in spots, especially when ulcers are present in the mucous membrane. The wall of the inflamed gall-bladder is almost always, however, of diminished resistance, friable, brittle, and readily torn. The mucous membrane usually

[1] Virch. Arch., 43 Bd., S. 289.

contains ulcers, and at times the entire inner surface consists of a large ulcerating surface. The contents sometimes consist of pure pus, sometimes they are mixed with bile, but almost always gall-stones are also present, perhaps in considerable number and size. These are usually freely movable, but at times they are situated in diverticulum-like recesses in the wall, which they have formed for themselves. The cystic duct is generally found impermeable.

Symptoms, Diagnosis.

The most important symptom, and one common to all forms of dilatation of the gall-bladder, is the presence of a tumor corresponding to the region of this organ, and extending, therefore, from the lower border of the liver downward and at the same time more or less to the right or left. This tumor is often detected by the eye, inasmuch as a flattened prominence can be recognized at the corresponding part of the abdomen. The extent and situation of the tumor, as well as its almost always pyriform figure (which grows smaller toward the border of the liver), can be determined by percussion. The tumor appears elastic, and more or less distinctly fluctuating to the palpating finger. Its lower portion can often be moved somewhat to the right or left side, and changes its position correspondingly when the patient passes from dorsal to lateral decubitus. Upon attempting to feel the boundaries of the tumor with the fingers, the former is readily displaced when strong and rapid pressure is exerted.

It cannot, by any means, be readily and certainly determined in all cases that the tumor belongs to the gall-bladder. Often, indeed, its shape and position are so characteristic that no doubt can arise, especially when the border of the liver can be readily felt and renders the examination easier. It is otherwise when there are anomalies in the shape and position of the liver which cause the gall-bladder not to assume its ordinary position, but to approach, perhaps, the axillary line, or to lie to the left of the median line of the abdomen.

When the tumor is exceedingly large, we would, at first, sus-

pect free ascites,[1] a cystic tumor of the ovary, perhaps a huge hydronephrosis, rather than dilatation of the gall-bladder, and it will require the most careful examination and judicious consideration of the symptoms in order to avoid mistakes in a concrete case.

As a matter of course not every swelling whose form and position correspond to the gall-bladder may, without further ado, be attributed to the latter. Echinococcus sacs and hepatic abscesses, which project in the vicinity of the lower border of the liver, cancers of the liver and gall-bladder may appear in a similar manner and give rise to mistakes. Echinococcus sacs, however, usually have a more hemispherical shape, as they project from the liver with a broad base, while the enlarged gall-bladder presents an elongated pyriform shape. But even an echinococcus sac may exceptionally appear in the shape of an elongated tumor, touching upon the liver by a narrow base, *i.e.*, it may simulate an enlarged gall-bladder. As painlessness and slow growth are peculiar to both tumors, or may, at least, occur in both, and as the hydatid-thrill is a very inconstant symptom of echinococci, confusion of both conditions cannot always be avoided. An hepatic abscess can be more readily differentiated from a tumor of the gall-bladder. The former constitutes a tumor which is primarily firm, then gradually grows softer, and which is combined with grave disturbance of the general condition (fever, chills, severe pains in the region of the liver, and often, also, in the right shoulder); the swelling in the former is also much broader and more diffuse. In dilatation of the gall-bladder, on the other hand, the tumor always presents the same resistance and elasticity, it can be more sharply defined from the beginning and has a more slender form, the pains and disturbance of the general conditions are absent or fall into the background, etc. Soft cancers, also, which proliferate at the lower border of the liver, may readily be mistaken for an enlarged gall-bladder. If we take into consideration, however, the more rounded form of the cancer, the multiplicity of the nodules usu-

[1] As in the often quoted case of Benson (the original source of which I have nowhere found mentioned), in which puncture of the abdomen was performed (under the false assumption of ascites), and nearly two quarts of biliary fluid were removed.

ally present in hepatic cancer, the nodular surface of the liver and the usually marked cancerous cachexia, a doubt can very rarely be entertained.

As soon as we are satisfied that the tumor which is present belongs to the gall-bladder, the further problem arises of determining its nature. The first question which arises is, whether the tumor is fluctuating or solid, *i.e.*, whether it is due to an accumulation of fluid in the gall-bladder, to cancerous degeneration of its walls, or finally, to an accumulation of gall-stones. The enlargements of the gall-bladder which are due to accumulations of fluid, almost always present themselves as fluctuating or, at least, elastic, often also movable, tumors, while cancerous and calculous growths almost always appear as hard swellings. The following factors should be taken into consideration in excluding the latter conditions:

The enlargement of the gall-bladder by an accumulation of gall-stones gives rise to a hard, sometimes knobbed or nodular tumor, which is usually movable and painless on pressure, although it may be the seat of disagreeable sensations of an undefined character. In palpating the tumor the sensation is sometimes experienced of a slight cracking or creaking, or the patient has a sensation, when he turns in bed, as if a firm body were moving from one part of the abdomen to another. Jaundice and other symptoms of gall-stones may have preceded, or may still continue, but all signs indicative of cholelithiasis may, with equal readiness, be absent and always have been absent. The size of the swelling remains stationary, or it increases very slowly and imperceptibly. When ulcerations occur in the mucous membrane of the gall-bladder, this picture may, indeed, be very appreciably changed. The signs of local peritonitis, especially severe pains, then develop over the site of the tumor, the latter becomes immovable and adherent, and its dimensions also visibly increase.

The cancer of the gall-bladder, on the other hand, represents a hard, sometimes nodular, tumor, which reaches the size of an orange, or may even exceed it. Even very soft cancers will, at least, allow considerable hardness to be felt in spots. Carcinoma of the gall-bladder is usually adherent, at all events not movable.

The growth appears tender on pressure, and is also generally the site of acute lancinating pains. As a rule, it rapidly increases in size; rapid emaciation and the other signs of cancerous cachexia become noticeable. Jaundice and vomiting are frequent symptoms in cancer of the gall-bladder. Such patients have generally suffered previously from gall-stones, or these still pass in the stools, especially when an ulcerative communication between the gall-bladder and intestinal canal has occurred from the spread of the cancer to the intestines.

Whether a fluctuating tumor of the gall-bladder contains bile, mucus, water, or pus, whether, then, a simple or dropsical dilatation or empyema of the organ is present, can be only surmised (without an explorative puncture)—at least, it cannot always be decided.

It should be regarded as simple dilatation, *i.e.*, an accumulation of bile in the gall-bladder, when icterus is at the same time present, which increases in intensity, while the evacuations from the bowels are completely discolored; when there is a general enlargement of the liver, tension and protrusion of the right hypochondrium, the signs of closure of the ductus choledochus and of retention of bile.

Dropsy of the gall-bladder may be accepted when jaundice, enlargement of the liver, painful sensations in it, and febrile symptoms are absent. However, certain exceptions to this rule may occur, as occlusion of the common excretory duct of the bile may be combined with previous closure of the cystic duct, and jaundice will then be associated with the older dropsy of the gall-bladder; the physician, however, not being able to follow these processes as separated in time, will fall into the error of regarding the gall-bladder as filled with bile, although it contains water or mucus. On the other hand, the gall-bladder may be immoderately filled with bile, although jaundice is not present (*vide* the above-mentioned valve-like action of gall-stones in the cystic-ducts); the physician will then suspect water in the gall-bladder, while it only contains bile. Fortunately, these errors, which are unavoidable under certain circumstances, possess no practical importance.

Empyema of the gall-bladder, especially that form which is

caused by occlusion of the cystic duct from the irritation of gall-stones, can be recognized from the fact that the tumor of the gall-bladder is the seat of markedly painful sensations and of greater tension than in simple dilatation by an accumulation of bile. To these are added febrile symptoms: heat, chilly sensations, or chills, and night-sweats. Empyema of the gall-bladder has all these symptoms in common with abscess of the liver, from which it is often differentiated with difficulty, or not at all, on account of the position and shape of the tumor. Special attention must therefore be paid, in making a diagnosis, to the clinical history. Empyema occurs especially in individuals who have suffered, or still suffer, from cholelithiasis, while abscess of the liver is a rare affection in temperate zones. Hepatic abscess is usually preceded by a general enlargement of the liver, due to hyperæmia and inflammatory processes, which belong as little to empyema of the gall-bladder as such, as the yellow color of the skin and discoloration of the stools.

The symptoms of inflammation which becomes associated with simple dilatation of the gall-bladder, will coincide, in general, with those of the latter, but the pains and tension in the region of the tumor become much greater on account of the inflammation, febrile symptoms are superadded, and the tumor rapidly increases in size.

Course, Duration, Terminations, Prognosis.

According to its causes, dilatation of the gall-bladder sometimes occurs in a short period, sometimes weeks and months elapse before it attains noteworthy dimensions. The dilatation due to occlusion of the ductus choledochus and empyema of the gall-bladder generally develops more quickly, and becomes more noticeable, on the whole, than true sacculated dropsy of the gall-bladder (due to closure of the cystic duct), which runs a very latent course, frequently becomes stationary, and then remains permanently unchanged, without any special annoyance and without the least danger to the patient. Apart from this favorable case, the disease may pursue a different course.

Dilatation of the gall-bladder may recover spontaneously,

and then again return to the normal condition. This occurs in simple dilatation after a duration of variable length, as soon as the cause of the occlusion of the ductus choledochus is removed. The inflammatory tumor of the gall-bladder (tumeur biliaire) has been often found to resolve, partly spontaneously, partly after the proper antiphlogistic treatment, even comparatively rapidly and completely. Experienced physicians, like Cruveilhier, Budd, Murchison, and others, consider the termination of this disease in recovery as very frequent, and even as the rule. This fortunate turn is explained by the fact that a calculus in the cystic duct may change its position, and again permit normal egress to the contents of the gall-bladder, or that the inflammatory swelling of the mucous membrane, giving rise to occlusion of the canal, subsides, and thus renders the passage free for exit and entrance. With the evacuation of the gall-bladder, one, if not the only cause of the cholecystitis also disappears, and recovery can then occur rapidly and completely.

In this respect, the oft-quoted case which is reported by J. L. Petit[1] is very instructive. Petit was requested, in a patient with a so-called tumor biliaris, which was regarded by the physicians as an hepatic abscess, to lay open the tumor by an incision. He had hardly cut through the skin when he noticed that the tumor moved and became smaller. He immediately desisted from the operation, and proceeded to unite the wound in the integument. To the astonished inquiries of the bystanders with regard to this remarkable conduct, he explained what he had noticed, and stated that in the supposed hepatic abscess he could only recognize an enlargement of the gall-bladder, due to the accumulation of bile. In fact, the patient immediately had to go to stool, discharged a large quantity of bile, and had entirely recovered in five days.

In other cases, however, the disease cannot be brought to a stand-still, but the tumor continues to grow, and sooner or later we are brought face to face with the threatening danger of an ulcerative perforation, or rupture of the gall-bladder. This danger is so much greater the more the walls of the gall-bladder are softened or otherwise degenerated by the inflammatory process. The ulcerative destruction of the mucous membrane, which occurs so frequently in empyema of the gall-bladder, due to the irritation of gall-stones, especially predisposes to rupture and

[1] Mémoires de l'acad. roy. de chirurg., T. I., Obs. III., p. 156.

perforation. But this phenomenon has also been noticed in simple dilatation from accumulation of bile. P. Frank observed a pregnant woman in whom the act of parturition was the exciting cause of rupture of the markedly enlarged gall-bladder, as this was adherent to the fundus of the uterus. The bile, which had escaped into the peritoneal cavity, was discharged externally through the vagina. I find no mention made of the further condition of the patient. In rupture of the gall-bladder, the contents of the latter usually pass into the peritoneal cavity, and cause a rapidly terminating, fatal peritonitis. If, however, adhesions of the gall-bladder to the surrounding parts have formed, as occurs especially in empyema of the organ, the spontaneous rupture may occur through the abdominal walls and skin externally, or into the intestines, and a biliary fistula then remains for some time, which may, under certain circumstances, close at a later period, after complete obliteration of the gall-bladder has occurred. Similar results are obtained when artificial evacuation of the gall-bladder is performed by puncture or by means of cholecystotomy.

Apart from the possibility of rupture, the patient is also exposed to danger, inasmuch as the continued secretion of pus and the ulceration of the mucous membrane of the gall-bladder may result in a hectic condition, with severe fever, rapid emaciation, profuse night-sweats, etc., to which the exhausted patient yields after a longer or shorter period.

The prognosis, therefore, assumes a variable character. It may be considered favorable as long as there is a possibility that the cause of the occlusion of the bile-duct can be removed ; furthermore, when there is no inflammation of the gall-bladder, or when it, and therefore the dimensions of the dilated organ, remain within moderate bounds. The prognosis becomes more grave when the tumor rapidly attains excessive dimensions, and when the inflammation in the sac increases in intensity. In true empyema of the gall-bladder, the prognosis is always extremely doubtful, and becomes almost fatal as soon as hectic symptoms make their appearance.

Treatment.

The treatment of simple dilatation from closure of the ductus choledochus is the same as that of jaundice, due to impermeability of this duct (*vide* the treatment of catarrhal jaundice and cholelithiasis). With regard to the other conditions now under consideration, an important problem for the physician consists in the careful treatment of any inflammatory symptoms which may appear on the part of the gall-bladder. The patient must carefully avoid bodily exercise, active movements, etc., must remain quietly in bed, and be subjected to a strict diet. Not alone the inflammatory symptoms, but even the tumor itself, and, therefore, the entire disease, have been often found to disappear under the use of warm poultices, inunctions of gray mercurial ointment, local abstraction of blood, and saline laxatives (severe straining at stool must be avoided, on account of the possible rupture of the gall-bladder).

If symptoms of impaction of gall-stones occur, they must be treated according to the rules holding good in such cases. We should then endeavor to render the passage of the calculi as painless as possible by the use of narcotics, warm full baths, etc.

If closure of the neck of the gall-bladder has really occurred, we find ourselves restricted to symptomatic measures. We should endeavor to relieve the most annoying symptoms, to regulate the passages from the bowels, aid digestion and preserve the energies of the body, on the whole, as much as possible. If the distention of the gall-bladder has attained such dimensions that the danger of rupture threatens, or if the organ is filled with pus and the symptoms of a wasting, hectic fever develop, the evacuation of the gall-bladder by puncture is indicated. This operation presents no danger if the gall-bladder is sufficiently adherent to the abdominal walls. If this is not the case, or we are in doubt with regard to the presence of sufficient adhesions, we must act in the same manner as is usually done in the operative treatment of hepatic abscess and echinococcus sacs, *i.e.*, we must artificially produce an adhesive inflammation by the application of Vienna cautery-paste, or by incisions into the abdominal walls down to the neighborhood of the peritoneum, etc.

As an important (sometimes the only) cause of the inflammatory irritation disappears with the evacuation and loss of tension of the gall-bladder, a single puncture, together with the thorough application of the other antiphlogistic remedies, may lead to permanent recovery. Repeated puncture is sometimes necessary, because the gall-bladder fills anew with inflammatory products. Finally, however, recovery occurs, either because the cystic duct becomes permeable and the cholecystitis subsides, or because (though the occlusion continues) at least the inflammation ceases and the sac grows smaller or is entirely obliterated.

Erdmann (Virch. Arch. 43 Bd.) observed in a musician, æt. twenty-four years, a dropsy of the gall-bladder, which occupied almost the entire abdomen, and which had grown to this size within eight months. Puncture was performed through the umbilicus, and the enormous quantity of 60–80 pounds of fluid, which looked exactly like bile, is said to have been discharged. The puncture produced complete evacuation. The attempt was made to prevent the recurrence of the fluid by the pressure of a bandage and quiet position. No inflammation developed in consequence of the puncture, but the return of the fluid could be proven in a week after the operation. Further information concerning the patient is wanting, but he is said to have been finally discharged cured. As no jaundice was present, the occlusion must have been situated in the cystic duct. It was probably a catarrhal swelling of the mucous membrane of this canal, as nothing indicated the presence of gall-stones, and recovery is, nevertheless, said to have occurred.

The above-mentioned case of Jacob (The Lancet, March 16, 1878, Vol. I., p. 383) referred to a man, æt. twenty-two years, who became affected with pneumonia after a fall upon the right side, and in whom (within ten days after the injury) a hard elastic tumor was noticed in the region of the liver, which extended to the umbilicus and projected six inches beneath the border of the ribs, without passing beyond the median line of the abdomen. Three days later the distinctly fluctuating tumor extended to the anterior superior spine of the ilium. Slight yellow color of the conjunctivæ, vomiting after meals. On the seventeenth day a trocar was passed into the most prominent part of the tumor, and five and a half pints of dark green bile were thus discharged. On the first day after the puncture a tumor could no longer be discovered beneath the ribs, but on the second day it had already returned, was indistinctly fluctuating, and extended to the umbilicus. As the tumor rapidly extended to the iliac fossa and to two inches beyond the linea alba, a fresh puncture was performed (twenty-fourth day), by which seven pints of mucous gall were discharged. One week after this second puncture the tumor again appeared, and extended to the ilium, but did not pass beyond the median line. At a third puncture (thirty-fifth day) eight and a

half pints of fluid similar to the former were removed. From this time recovery of the dilatation began, the previously pale stools became progressively darker, but the patient was only discharged as entirely cured after several weeks.

When the case is not merely one of biliary or purulent fluid in the gall-bladder, but gall-stones are, in addition, also present and do not permit the cholecystitis to recover, but especially when extensive and deep-seated ulceration of the mucous membrane of the gall-bladder is present and is maintained by the abnormal contents of the organ, we can, at the most, expect from the puncture a temporary relief but no radical cure. In such cases cholecystotomy,[1] *i.e.*, a free opening into the gall-bladder by incision, which permits thorough evacuation of the gall-bladder, is indicated as a last resort. This operation, which had been already thoroughly discussed by J. L. Petit in his celebrated treatise on biliary tumors (*vide* literature), appears to have been performed but rarely and with but slightly encouraging success, else it would hardly (although entirely rational) have sunk into oblivion for such a long period as it really did. Only very recently has cholecystotomy, with the technical aspects of which we are not now concerned,[2] been again practically carried out, and in part with good success. The brilliant results of ovariotomy, and the greatly diminished dangers of the operation under Lister's antiseptic method, may perhaps tend to bring cholecystotomy again into vogue.

Marion Sims operated, in April, 1878, upon an American woman forty-five years of age. Thick bile and, after a while, nearly sixty gall-stones were removed from the gall-bladder. Recovery occurred without interruption, and the annoying symptoms disappeared immediately after the operation. But grave symptoms developed six days afterward: hemorrhages from the mucous membrane of the gall-bladder, the tongue and gums, against which injections of ergotin, chloride

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[1] Cf. *Nussbaum*, Verletzungen des Unterleibes (*Billroth* u. *Luecke*, Deutsche Chirurgie, 1880, 14 Lief., S. 86 ff.). I find quoted, though I could not obtain the original: *Herlin* (1767), Expériences sur l'ouverture de la vésicule du fiel et sur son exstirpation dans le chien et le chat. Expériences répétées par l'Anglas. Ligature du canal cystique, et exstirpation de la vésicule sur des animaux qui guénent (véritable pathologie expérimentale trés-remarquable pour l'époque). Journ. de Roux. Juillet, T. XXVII., p. 403.

[2] *Vide* the cases of operation at the close of our list of the literature.

of iron, etc., proved useless. Hæmatemesis followed, the vital energies sank, and death occurred eight days after the operation. Autopsy: Abdominal wound entirely healed, no sign of peritonitis, sixteen calculi, from the size of a pea to a pigeon's egg, still remained in the gall-bladder, and were all imbedded in diverticulum-like recesses of its walls. The wall of the markedly enlarged gall-bladder was considerably thickened and very firm. Abundant coffee-grounds-like masses in the stomach and duodenum. It therefore appears as if the operation, which was in itself successful, had been performed in a stage of the disease which was already too far advanced.

In June, 1878, Kocher operated with complete success upon an empyema of the gall-bladder as large as a man's head in a woman æt. thirty years. The wall of the sac was about 1 ctm. thick. The gall-bladder contained pus of a suspicious odor; thirty-two gall-stones were soon removed by irrigation and changes of position. No fever developed, and the patient was able to rise within three weeks. As a fistula was still present, it was dilated with laminaria and sounded. No large cavity was found, but some gall-stones were noticed which were firmly embedded in irregular recesses in the walls. In three séances occurring at intervals of two days, six, three, and two calculi respectively were extracted. The fistula closed since then; no bile had been discharged at any time. It was therefore supposed that the cystic duct was entirely obliterated, while the hepatic duct and ductus choledochus were free and permeable.

The successful case of G. Brown (early part of 1878), referring to a woman æt. forty-five years, cannot, strictly considered, be regarded as cholecystotomy, as the operation was discontinued after incision of the abdominal walls, because the gall-bladder was covered by the thickened omentum, and the operator, as it seems, thus lost his bearings, and with them his confidence. The abdominal wound was then closed, but on the following morning the bandage was so saturated with biliary fluid, that at least a pint must have escaped. It was therefore a spontaneous rupture of the gall-bladder, but occurred under such fortunate circumstances, that the contents of the organ found an exit through the abdominal wound, and the peritoneum escaped. The flow of bile continued for a few days, when it became purulent and foul-smelling. But this only continued for a short time; the discharge disappeared, and recovery occurred, a fistula remaining. The latter closed in three to four months after the operation, and since then the patient has enjoyed excellent health. Keen's case (a woman, æt. sixty years) proved fatal thirty-six hours after the operation.

The latest case (August, 1879) of Lawson Tait, in a middle-aged woman, also had a favorable termination. A firm, elastic tumor without fluctuation, tense, and movable in all directions, was felt in the region of the gall-bladder. Although the diagnosis remained doubtful, an operation was decided upon. The abdomen was opened in the median line by an incision four inches in length. The tumor was now recognized as the gall-bladder; it contained a whitish, opaque fluid and two large calculi, one lying loose, the other impacted in the neck of the gall-bladder, and firmly adherent to the mucous membrane. The latter was

not removed without difficulty. The patient rapidly recovered after the operation; the escape of bile from the wound continued for two weeks. Five weeks after the operation the patient had entirely recovered.

Appendix.

Dilatation of the Bile-Ducts.

Every occlusion of the bile-ducts leads to a corresponding dilatation of those portions of the system of biliary canals which are situated farther back. As a rule, the gall-ducts are then diffusely dilated, but are also provided, at times, with ampulla-shaped recesses. It has been previously mentioned that the dilatation of the ductus choledochus may attain the size of the intestine. Trafflemann, indeed, reports a case in which the ductus choledochus, which was filled with calculi, was as wide as the stomach. Mention has also been made of the primarily biliary, then watery mucoid contents of such dilated gall-ducts.

If we find a dilatation of the bile-ducts without any mechanical obstruction, the conclusion is warrantable that such an obstruction has previously existed, and that, after its removal, relaxation of the duct remained, so that it could not again return to its original size (Frerichs).

Within the liver sacculated cavities, true cysts, may form from the occlusion of individual ducts. They are of a rounded shape, closed, provided with thick fibrous walls, and filled with a viscid fluid, with a biliary "gruel," with calculi, or also with a more serous fluid.[1] They are usually of small size, but exceptionally they become as large as a pigeon's egg.

The effect of these conditions upon the hepatic tissue, viz., compression and disappearance of the latter, finally complete degeneration of the parenchyma, etc., have been previously considered among the sequences of occlusion of the bile-ducts.

In addition, we shall make a short reference to certain rare forms of sacculated dilatation of the large biliary excretory ducts

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[1] *Vide Cruveilhier*, Anatomie pathologique, Livr. XII., Pl. IV., Fig. 3.

outside of the liver,[1] but which barely present more than an anatomical interest.

The specimen from the Breslau Anatomical Museum, described and drawn by Frerichs,[2] may serve as a type of these formations: The gall-bladder is normal in shape. The neck of the bladder leads into a wide membranous sac, eight inches long and five inches wide, filled with thin bile, and which proved to be the greatly dilated cystic duct and ductus choledochus. The sac extended to the duodenum, but was here entirely closed. The situation, at which the ductus choledochus opens, was marked by a slight prominence in the interior of the duodenum. The mouth of the pancreatic duct was free. No boundary could be discovered between the cystic duct and the ductus choledochus, as both were equally dilated; it was only indicated by the entrance of the hepatic duct into the sac.

Albers represents a specimen very similar to the one just described in Plate XXXVI., Fig. I. of his atlas (Part IV.). The ductus choledochus here presents the size of a large orange, and has a firm, fibrous wall over 1 ctm. thick.

The conditions are similar in the case described by Barlach:[3] a thick-walled cyst, almost as large as a child's head, was adherent to the lesser curvature of the stomach over an extent of 11 ctm. This communicated freely with the stomach by a perforation 6 ctm. long; it contained bile and a small piece of wheat bread. The atrophied gall-bladder formed an appendage of the upper part of the cyst, and communicated with the latter by a small opening; the hepatic duct also emptied into the same opening. The ductus choledochus was surrounded and occluded by a fleshy tumor (*i.e.*, only its lower end, while the upper portion was dilated to form the cyst).

Disturbances in the Continuity of the Biliary Passages.

(*Perforations, Ruptures, Fistulæ.*)

Leseure, Sur les ruptures et les perforations de la vésicule biliaire. Paris, 1824.—*Fauconneau-Dufresne*, Traité de l'affect. calcul. du foie, etc. Paris, 1851, p. 293 ff.—Dictionnaire encyclopéd. des scienc. méd. Ed. by Dechambre (Art. Voies biliaires by Barth and E. Besnier), 1868. T. IX., p. 372 ff.—*Murchison*, Clinical Lectures on Diseases of the Liver. 2 ed. 1877, p. 497 ff.—*Vide* also

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[1] *Vide* also *Raynaud* and *Sabrina*, Enorme Erweiterung der Gallenwege, etc.; Arch. de physiol., 2 sér. VI., p. 37, Janv.–Févr., 1879.

[2] Klinik d. Leberkrankhtn., II., S. 443.

[3] Ein merkwuerdiger Fall von Verschluss des Duct. Choledochus. Deutsche med. Wochenschr., No. 31, 1876.

the corresponding sections in the surgical handbooks, especially *Nussbaum*, Verletzungen des Unterleibes (Billroth und Luecke, Deutsche Chirurgie, 1880, 14 Lief, S. 86).

1. *Perforations of the Biliary Passages.*

Pathogeny and Etiology.

Ulcerative perforations of the biliary passages occur in the course of more than one diseased process. If we entirely disregard traumatic perforations, they may be divided into two groups; in one the contents of the gall-ducts escape into the abdominal cavity or into enclosures which have developed accidentally within the peritoneal sac (encapsulated purulent and ichorous foci); the perforations of the second group, on the other hand, only occur after previous adhesion of the affected gall-duct to the adjacent parts, and place the bile-ducts in communication with one of the neighboring hollow organs, or permit the bile to escape externally, after perforation of the abdominal walls. The first group represents perforations in the narrower sense, the second bear the name biliary fistulæ.

Perforations, in the stricter sense, may develop at any part of the biliary system; they occur in the small subserous dilatations of the peripheral hepatic ducts, as well as in the large excretory ducts outside of the liver, but especially in the gall-bladder.

In the canals situated within the liver the perforation sometimes occurs from within outward, sometimes in the opposite direction. The first form occurs in dilatation of these canals in consequence of biliary stasis, in inflammation and ulceration of the canals, from the presence of foreign bodies (concretions, round-worms, etc.). The second form develops from the spread of inflammatory and ulcerative processes from the hepatic tissue to the walls of the bile-ducts, from the opening of echinococcus sacs into the ducts, the discharge of the contents of abscesses, etc.

In the excretory bile-ducts outside of the liver, the perforation occurs, as a rule, from without inward, and is then almost always the result of an ulcerative cholangitis, which has its primary cause in the presence of gall-stones, round-worms in the

ducts, etc., or in a cancerous degeneration of the duct. Among the factors which are followed by perforation of these ducts from without inward, we may mention carcinomatous neoplasms (for instance, of the duodenum), aneurisms of the abdominal arteries, echinococcus sacs and purulent or gangrenous foci in the immediate neighborhood of the ducts.

Perforation of the gall-bladder also occurs, as a rule, from within outward. Its usual starting-point is an ulcerative cholecystitis, and it is immaterial whether this is due to the presence of gall-stones, of a typhoid affection, or what not. It is peculiar to the history of cholecystitis calculosa, as well as of cancer of the gall-bladder, that an adhesive peritonitis develops more readily than in certain other forms of ulcerative cholecystitis, and leads to adhesion of the liver to the adjacent organs; therefore, perforations due to the first-mentioned cause often lead, not to perforation into the peritoneal cavity, but rather to the formation of biliary fistulæ. On the other hand, simple ulcers of the gall-bladder, which are caused by gall-stones, and typhoid ulcers of the organ often pursue an entirely latent course, and, without having given rise to an adhesive peritonitis, they burst suddenly and unexpectedly into the peritoneal cavity, so that the fatal peritonitis acutissima first leads us to think of the possibility of an ulcer of the gall-bladder.

As soon as the perforation has become complete at any part of the biliary passages the contents are discharged externally; a free escape of bile occurs, or, if there are obstructions, a biliary infiltration of the tissues, with which the discharging bile first comes in contact.

If the rupture occurs into the interior of the liver, under certain circumstances no bile may make its appearance, but it can remain enclosed in the parenchyma of the organ (somewhat after the manner of a cerebral hemorrhage), and thus forms a biliary apoplexy within the organ. If the rupture of the hepatic bile-ducts occurs into an abscess, an echinococcus sac, or into a large blood-vessel, the discharge of blood and pus, or the contents of the hydatid cysts, will be added, in the opposite direction, to the outflow of bile. This occurrence often has a favorable influence upon the abscess or echinococcus sac, while a dangerous

process develops almost necessarily in the blood-vessels. In other cases, in which the perforation is the result of an ulceration of the bile-ducts caused by gall-stones or round-worms, purulent cavities may form in the hepatic tissue from extension of the inflammation to the latter, in which even calculi or ascarides have sometimes been found. Such cavities should not be mistaken for dilatations of the gall-ducts.

On the other hand, when the gall-bladder, or one of the large excretory ducts, is the site of the perforation, and the bile finds a free escape into the abdominal cavity, it may accumulate here in enormous quantities. The discharge of bile immediately produces the most severe symptoms of peritonitis, which, with scarcely an exception, runs a rapidly fatal course. This phenomenon occasionally occurs in patients suffering from gall-stones during the course of an especially severe attack of hepatic colic, when not alone the escaped bile, but sometimes, also, the gall-stone, which produced the occlusion, are found in the abdominal cavity. Similar observations have sometimes been made when the occlusion of the bile-ducts was due to round-worms.[1]

If, as has also been observed, we find free escape of bile within the abdominal cavity, although the anatomical signs of peritonitis are not present, we must then conclude that the perforation or rupture occurred immediately before or even at the time of death, perhaps even after life had ceased.

During the slower course of those processes which prepare the way for perforation of the bile-ducts, local inflammation and adhesion of the parts to one another may form at the site of the future rupture. When the adhesions arising in this manner are sufficiently firm and extensive, the perforation which occurs later does not permit the free escape of bile, but, at the most, a more circumscribed infiltration of bile in the region of the peritoneal adhesions and false membranes, and the otherwise so dangerous occurrence may terminate in a favorable manner. However, it also happens, as, for instance, in incomplete perforation of the wall of the gall-bladder, that the bile, which is infiltrated into

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[1] *Vide Davaine*, Traité des Entozoaires, 2 éd. 1877, pp. 164 and 165. *Vide* also the chapter, which will follow later, on Ascarides in the Biliary Passages.

the meshes of the connective tissue and between the individual layers of the gall-bladder, is diffused over a wide surface, and severe disturbances and even a fatal peritonitis may nevertheless develop. It occurs still more frequently that, despite the adhesions present between the organs of the abdomen, a true, though circumscribed effusion of bile takes place (after the manner of an encapsulated exudation) which occasionally forms a tumor as large as a child's head. These cases also generally terminate by the supervention of fatal peritonitis. These encapsulated extravasations of bile develop, by preference, during the course of typhoid diseases, especially when gall-stones are present at the same time in the gall-bladder. However, it follows from the sometimes long duration of these extravasations, that the peritoneum does not tolerate the contact of bile as poorly as is generally maintained.

Symptoms and Diagnosis.

The symptoms by which perforations of the biliary passages are announced vary according to the different circumstances under which they develop. If the perforation occurs suddenly, and a large quantity passes at once into the abdominal cavity, this takes place with the same symptoms as in true rupture of the biliary passages (*vide* this affection). If the perforation occurs into the inside of the liver, there may not be a single symptom which points in this direction. At the most, in rupture of abscesses, especially of echinococcus sacs, a conclusion may be drawn with regard to the process within the liver from the passage through the intestines of substances derived from the contents of the former.

Those perforations which develop in the large excretory ducts outside of the liver, and in the gall-bladder, and which are accompanied by inflammatory processes under the form of pericholecystitis, perihepatitis, or pericholangitis, produce the symptoms of perihepatitis or of peritonitis, which is sometimes circumscribed, sometimes diffuse. Exceptionally, they also appear under the form of an extremely acute general peritonitis, or of a perforation-peritonitis in general. The latter always occurs when

the perforation takes place suddenly, without previous inflammation and attempts at adhesion, and gives rise to a copious, free exudation of bile into the abdominal cavity. It is readily understood, on account of this agreement of the symptoms, that many cases of perforation of the biliary passages are regarded as intestinal perforations, and that the autopsy alone can clear up the true state of affairs. The confusion of these conditions is so much more readily possible, as perforation of the biliary passages occurs, in great part, in individuals who are otherwise apparently healthy, or at least in the course of those diseases which very often give rise to intestinal perforation, as is especially true of typhoid fever. If the perforation develops latently, the diagnosis, after its actual occurrence, can, at the most, rely upon the situation in which the pain was first observed, and upon the site of the other subjective sensations which may be combined with perforation of the peritoneum. But as no great weight can be attached to such impressions of the patient, the diagnosis will usually not possess more value than that of a more or less probable surmise. The diagnosis of perforation will present less difficulty in the numerous cases in which it is a sequence of gall-stones. In every case in which cholelithiasis can be determined from the previous history of the patient, or in which the passage of gall-stones in the stools has been actually observed, we can make a diagnosis of perforation of the gall-bladder, or of the large excretory ducts, with a high degree of certainty, in case the local symptoms are in accord.

Terminations and Prognosis.

In the large majority of cases perforation of the biliary passages causes death, usually in a very short time, and probably always in those instances in which a large and free exudation of bile has occurred into the abdominal cavity. Recovery can only occur exceptionally when the effusion of bile remains within moderate limits, and the extravasation is converted into a sacculated deposit by firm false membranes. The prognosis depends chiefly upon the intensity and extent of the peritonitis, and upon the acuteness of its development. In general it must be regarded

as fatal. The prognosis should be very reserved even in encapsulated extravasations of bile, as the condition may take an unfavorable turn at any moment from the spread of the inflammation to the previously unaffected portions of the peritoneum.

Treatment.

The treatment of perforation of the biliary passages coincides, in the main, with that of perforation-peritonitis in general. The general condition of the patient, and the prominence of individual symptoms will furnish the special indications. As a rule, we will have to resort to local antiphlogistic measures (leeches in the region of the gall-bladder, poultices, or even an ice-bag upon the painful right hypochondrium, etc.), and especially to opiates in very large doses. In addition, everything which might tend to increase the secretion of bile, as, for instance, copious drinks and all active movements, must be avoided. Everything must be removed which could stimulate and maintain intestinal peristalsis, the patient must maintain absolute bodily rest, and in the medical examination the physician should spare the patient, and especially the painful parts of the abdomen, as much as possible.

2. *Ruptures of the Biliary Passages.*

Ruptures of the biliary passages may occur occasionally in any portion of this system, but those of the gall-bladder and large excretory ducts must be mentioned as by far the most important and frequent. Purely traumatic ruptures occur very rarely in the parts mentioned; the cases are somewhat more frequent in which the rupture is favored by pathological conditions of the biliary passages, as, for instance, extreme dilatation of the gall-bladder by fluids, inflammatory and ulcerative processes, which have deprived the walls of the gall-bladder and ducts of their original powers of resistance. In such cases a comparatively slight mechanical force, a contusion of the hepatic region, straining during delivery, etc., may suffice to cause rupture of these parts. The same force would not have produced this result, if it had affected the perfectly healthy gall-bladder.

Ruptures which occur under such circumstances, and in which, therefore, the aid of other violent influences is absent or overlooked, are generally termed spontaneous ruptures.

The following case[1] would present a remarkable example of spontaneous rupture, if the observation were complete:

A man, æt. twenty-five years, previously healthy, awoke early with severe pains in the epigastrium and right hypochondrium, together with tenesmus, though no evacuation followed. Within one to two hours emesis of a brown, stercoraceous fluid set in, with continually increasing intensity of the pains. Urine and fæces entirely absent. Pulse very small, almost imperceptible. Death after the sickness had continued fifty-eight hours. Autopsy: several quarts of dark green fluid in the peritoneal cavity. The peritoneum around the liver and the omentum of a bright yellow color. Gall-bladder empty. The ductus choledochus is ruptured for a distance of three-fourths of an inch near its entrance into the duodenum, just at its union with the pancreatic duct. As the patient lived in extreme poverty, M'Swiney believes that the want of food caused the cessation of the discharge of bile, and, in this manner, rupture of the bile-duct.

In traumatic, as also in those spontaneous ruptures in which no inflammatory adhesions of the biliary passages with adjacent organs, preparing the way for the separation of continuity, have preceded, the bile escapes freely into the abdominal cavity at the time of rupture. This happened in Wolf's case.[2] A complete transverse rupture of the hepatic duct occurred, and both ends of the duct were found floating in a mass of semicoagulated blood. The abdominal cavity contained a free biliary effusion in enormous quantity, as it had been preceded by biliary stasis in consequence of the impaction of gall-stones. Matters present a similar appearance in rupture of the gall-bladder, if this happens to be dilated to a great degree.

The sudden and copious effusion of bile into the abdominal cavity, which accompanies the act of rupture, gives rise to the symptoms of the most acute diffuse peritonitis. Intense pains, which rapidly increase and become unendurable, starting from the region of the liver and soon spreading over the entire abdomen, extreme tenderness of the abdomen on contact, enlarge-

[1] *M'Swiney*, Rupture of the Biliary Duct. Dubl. Jour. of Med. Sc. Nov., 1866. Cf. *Virchow* and *Hirsch*, Jahresbericht f. 1866. II. S. 144.

[2] *Vide* Graefe's Journ. 12 Bd., S. 370.

ment of the abdomen, sometimes vomiting, furthermore syncopal attacks or true unconsciousness, disturbed and anxious expression of the features, collapse, low temperature of the extremities, small and very frequent pulse, retention of urine, etc.—point to the dangerous condition which has just developed. According to the duration of the disease, which, as a rule, hardly extends beyond twenty-four to forty-eight hours, the anatomical changes peculiar to peritonitis are found more or less marked upon autopsy.

We have referred above to the fact that the prevalent opinion, according to which the bile has the significance of a severe poison upon the previously healthy abdomen, is not placed beyond doubt. In fact this question, which does not, by any means, appear to be ripe at the present time, deserves an exhaustive study from the standpoint of clinical experience as well as on the basis of pathological experiments. So much has been observed, that the contact of bile with the peritoneum may be tolerated for a number of days, and that, even during this time, changes develop in the peritoneum which appear suited to inaugurate a healing process.

Thus, Thiersch,[1] for example, reports a rupture of a large bile-duct in a young man whose abdomen had been pressed against a wall. For two weeks he was not confined to bed, and then moderate jaundice appeared with considerable effusion into the abdomen. Several punctures furnished each time from nine to twelve litres of fluid, of which four-fifths were bile and one-fifth serous transudation. Death occurred from inanition. The peritoneum was covered by a membrane of uniform thickness throughout, which could be removed as a whole, and had imbibed bile on the surface, but was colorless more deeply (from absorption). Thiersch explains the icterus by this absorption.

Apropos of this report, it was remarked in another quarter (Lesser) that large extravasations of bile, which are introduced experimentally into the abdomen of dogs, do not produce peritonitis. If this should be corroborated, we may, in the future, indulge the hope that the conditions at present under consideration may prove accessible to treatment by surgical means.[2]

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[1] Cf. Berl. klin. Wochenschr. 1879. No. 23, p. 345.

[2] *Vide* also the propositions by *Nussbaum*, in Deutsche Chirurgie. 14 Lfg., 1880.

The remarks made concerning perforations will apply, with unimportant modifications, to the diagnosis, prognosis, and treatment of rupture of the biliary passages.

3. *Biliary Fistulæ* (*fistulæ biliariæ*).

Pathology and Etiology. Pathological Anatomy.

By biliary fistulæ we mean the abnormal communications between the lumen of the biliary passages and any other hollow organ lined with a mucous membrane, or with the surface of the external integument, which permit the escape of bile externally, either immediately through the abdominal walls or mediately through an adjacent hollow organ (intestine, etc.). As a rule, biliary fistulæ are the result of an ulcerative process starting from the mucous membrane of the biliary passages, in the course of which an inflammatory adhesion of the bile-duct occurs with an adjacent organ, and furthermore, an ulcerative perforation of the wall of the bile-duct and also of the organ adherent to it. Exceptionally, biliary fistulæ may also be left over after perforating wounds of the abdominal walls and gall-bladder (gunshot and incised wounds).

The fistula presents itself as an ulcerated passage of very variable width and length, of a straight or curved course. It is sometimes direct, *i.e.*, the wall of the bile-duct, at the perforated spot, is directly united to the abdominal or intestinal walls, etc., so that the opening constitutes a simple hole; or, and this is more frequently noticed, the fistula is indirect, inasmuch as it presents two openings, which are connected by an ulcerated passage of greater or less length. Sometimes even a true cavity, or cloaca, is inserted between the two openings of the fistula. When this is the case, a cloaca or encapsulated extravasation of bile was first formed after the perforation of the biliary passages, and not until later did the rupture of the latter through the adjacent organ (and thus the second opening of the fistula) take place.

The starting-point of most fistulæ is situated in the gall-bladder, more rarely in the bile-ducts within the liver, or in a localized

lesion communicating with them; most rarely the fistulæ start from the large excretory ducts outside of the liver.

According to the direction taken by the biliary fistulæ, and according to the organs which are thus placed in abnormal communication with the bile-ducts, they may be divided into several groups. In this respect we differentiate:

1. Fistulæ which place the biliary passages in communication with the stomach or intestinal canal, especially with the duodenum or large intestine (so-called gastro-intestinal biliary fistulæ).

2. Fistulæ which lead from the biliary passages to the urinary passages or genitalia (fistulæ biliariæ genito-uriniariæ).

3. Fistulous communications between the lumen of the biliary passages, and that of the trunk or branches of the portal vein (so-called circulatory biliary fistulæ), which, however, when strictly considered, are not included under this category.

4. Fistulæ which give rise to a communication of the biliary passages with the air-passages or bronchi (bronchial biliary fistulæ).

5. Fistulæ between the biliary passages and the outer surface of the body (so-called cutaneous biliary fistulæ).

Practically the cutaneous and gastro-intestinal fistulæ are by far the most frequent and important; all other forms represent very exceptional occurrences.

a. *Gastro-intestinal biliary fistulæ.* They usually occur between the gall-bladder and the duodenum or the transverse colon, much more rarely between the gall-bladder and stomach. They may, however, also lead from the large excretory ducts, especially the ductus choledochus, to the stomach and intestines. The fistulæ which connect the duodenum or transverse colon with the gall-bladder, are sometimes direct, the walls of both organs are in close apposition and adherent, and the fistula forms a simple hole through which both cavities communicate. In other cases a cavernous space is found inserted between both openings of the fistula—a sort of cloaca of larger or smaller dimensions, which is enclosed in the adherent adjacent parts. The fistulous opening itself usually possesses a quite considerable diameter; this is especially true of direct fistulæ, which sometimes constitute an opening as large as a Mark or a dollar.

Apart from the rare cancerous fistulæ,[1] almost all internal biliary fistulæ must be attributed to gall-stones, which produce an ulceration of the biliary passages, leading in time to perforation. As a rule, therefore, gall-stones (especially those of large size) pass through these fistulæ, and at a later period often give rise, on account of their large dimensions, to the symptoms of obstruction of the bowels.

With reference to the further fate of gastro-intestinal biliary fistulæ, they remain stationary in many cases during the entire period of life, especially when the cystic duct is patent and the flow of bile therefore continues through the opening. But it cannot be doubted that such fistulæ may, at a later period, close and become entirely obliterated, so that of the former fistulous communication only a solid fibrous band remains, the ends of which are connected with the two cicatrices of the mucous membranes.

The symptoms of gastro-intestinal biliary fistulæ are so slight and are usually concealed to such an extent by the inflammatory symptoms accompanying their development, that a diagnosis can never be made during life. There is reason to suspect the presence of such a condition when a gall-stone of unusual size passes per anum, or when the severe symptoms of obstruction of the bowels have been caused by such a concretion. The existence of the biliary fistula is so much more probable when a large gall-stone has entered the intestine, although its passage has not been accompanied by severe attacks of hepatic colic. If a gall-stone is expelled by vomiting, the assumption of a biliary gastric fistula is so much more plausible, the larger the calculus is and the slighter the disturbances which preceded its expulsion. But Cruveilhier undoubtedly goes too far when he regards the vomiting of gall-stones as positive proof of the existence of a biliary gastric fistula, as there is a possibility that the calculus has passed backward from the duodenum into the stomach. In like manner we may be led to assume a duodenal or colon biliary fistula from the discharge of large gall-stones per anum, but this presumption is not necessarily correct, because concretions of quite considerable

[1] *Vide* the observation of a cancerous fistula of the gall-bladder and transverse colon, by *Murchison*, Path. Trans., Vol. VIII.

size may pass in the natural manner through the strongly dilated ductus choledochus.

b. *Biliary fistulæ*, which empty into the *urinary passages*. I find only three cases of this kind mentioned in literature, of which, moreover, only the first was demonstrated on autopsy. In all the cases the formation of the fistulæ was caused by gall-stones.

1. Faber-Koestlin's case.[1] A previously healthy woman, in the middle of the thirties, was attacked by bladder disturbances, and within three years passed fourteen cholesterine calculi, four of which were large and weighed about three grammes each; the other smaller, weighing each about one-half gramme. Health was restored after the passage of these biliary calculi from the bladder. The patient died about twenty-five years afterward at the age of sixty-three. The autopsy performed by Koestlin gave the following results: Liver normal, but pressed somewhat downward. From the middle of its lower border a round cord extended to the fundus of the urinary bladder in front of the intestines, and especially pressed the transverse colon downward and to the left. This cord consisted of two different parts; the inferior larger half was formed by the urachus, the upper and longer half belonged to the gall-bladder. This was more than three inches long, and became narrower inferiorly, where the inside was lined by longitudinal folds situated closely together. No calculi were found either in the gall-bladder or urinary bladder. The urachus, which was loosely adherent to the lower end of the gall-bladder, continued its course as usual from this point to the bladder, and was permeable throughout its entire length.

2. Pelletan-Barraud's case (Journ. de Chimie méd. 2 Sér., T. II., No. 11 and 12, quoted by Koestlin). This case was not corroborated by autopsy. A woman, æt. thirty-six years, complained for two years of a dull, painful sensation on the right side above the iliac fossa. After these symptoms had diminished, prolonged vesical tenesmus suddenly developed. Two months later a large number of calculi fell with a loud noise into the pot de chambre, and about two hundred of these concretions were passed within a week. A large calculus remained in the urethra, and it became necessary to withdraw it. The concretions contained ninety-five per centum cholesterine. A sensation of weight was left over in the right side. The urine appears never to have contained biliary constituents. Jaundice was not present.

[1] *H. Faber.* Ueber den Abgang von Gallensteinen durch die Harnwege. Diss. aug. Tübing. 1839. (The same case is described in the Heidelberger med. Annalen, 1839, Bd. V., and in Schmidt's Jahrb., 1840). The patient in question died in 1863, and the autopsy was made by Koestlin. *Vide* Deutsche Klinik. 1864, p. 116. *Murchison* (Clin. Lectures, 2d ed., p. 500), being led astray by a statement of Fauconneau-Dufresne, incorrectly states that, in the Faber-Koestlin case, the gall-bladder was adherent to the pelvis of the right kidney, which must be rectified according to the above account.

3. Gueterbock's case[1] (Virch. Arch. f. p. A. LXVI., p. 273). A previously healthy woman, æt. fifty-six years, began to suffer from urinary disorders. Examination of the urinary bladder showed the presence of several calculi. With the aid of Lueer's forceps, several calculi, nearly as large as nuts, were removed piecemeal in four sittings. They consisted in the main of cholesterine and had a thin covering of urates. The patient is still living, and has never presented symptoms on the part of the biliary passages, etc.

Our experience concerning fistulous communications between the biliary passages and genital organs is confined to the previously mentioned observation by J. B. Frank ("Observ. med.-chir. Magunt," 1873). He reports a case of adhesion of the gall-bladder to the uterus in a pregnant woman. During the act of parturition rupture of the gall-bladder occurred with periuterine effusion of bile and perforation of the vagina.

c. The so-called *vascular biliary fistulæ* will be more properly discussed under the head of pylephlebitis. The rupture of an ulcer of the biliary passages into the adjacent trunk or branch of the portal vein, and the passage of bile and gall-stones into these blood-vessels is a rare occurrence, which refers, in so far, to the biliary passages, with which at present we are alone concerned, as an extravasation of blood into the latter may be combined with it. We find quoted everywhere the observation of Realdus Columbus, who observed, in the portal vein of Ignatius Loyola, three gall-stones which had entered from the gall-bladder; also the observation of Jacob Camicenus, who found the portal vein filled with gall-stones, while a calculus of the same kind still lay in the ductus choledochus. Cases of ulcerative communication between the bile-ducts and portal vein, belonging to this category, are reported by Dance, Budd, Lebert, Devay, Luys, and others, and have been previously referred to under the head of cholangitis.

d. Fistulæ between the *biliary passages and air-passages* develop with so much more difficulty, because the large bile-ducts are situated near the under surface of the liver. I have only run across two observations belonging here. Dr. Cayley (Path. Trans., Vol. XVII., p. 161, 1866) gives a report of a so-called pleural biliary fistula. An abscess-like cavity had formed between the diaphragm and the left lobe of the liver, and was

[1] *Vide* Berlin. Klin. Wochenschr., 1871, No. 49 and 51, and Virch. Arch. f. path. Anat. LXV., pp. 410 and 414.

connected on one side with a large hepatic bile-duct which was dilated like a cyst, and on the other side, with the left pleural cavity by a canal as thick as a quill. About a litre of bile mixed with pus was present in the latter cavity. A true bronchial biliary fistula was recently described by Dreschfeld.

The case is remarkable from the fact that the most striking symptom was the expectoration of large masses of bile with the sputum, although no jaundice was present; after the death of the patient a calculus was found near the upper surface of the liver, which had caused the fistula between a large bile-duct and the lung. The autopsy of the patient, a man æt. sixty-two years, showed the following: The right lung and liver bound to the diaphragm by old adhesions. The lung and liver were inseparably united at the centrum tendineum, which was converted into a white callous mass half an inch thick. The liver normal in size, the cystic duct closed, the gall-bladder dilated by colorless mucus (but no calculi). On section of the liver some bile-ducts are found normal, others dilated and filled with thick, yellow pus. They are connected with a small cavity near the superior surface of the liver, lying underneath the centrum tendineum (in a condition of fibrous degeneration) and containing similar thick pus. This cavity enclosed a gall-stone. A sinuous canal led from the cavity to the lung, where it communicated with a bronchus. The walls of the fistulous passage were firm and callous; the ductus choledochus was permeable.

The fact that the gall-stone was the cause of the pulmonary biliary fistula makes this case unique, as fistulæ of this kind, characterized by the discharge of large quantities of bile with the sputum, have been several times found to start from hepatic abscesses or echinococcus cysts, which first ruptured into a bile-duct, and thence, at a later period, through the diaphragm into the lung.

e. Cutaneous or *external biliary fistulæ* are due almost exclusively to gall-stones, exceptionally to wounds of the biliary passages or to hepatic abscesses, which rupture through the abdominal walls and communicate with a gall-duct. The number of known cases of external biliary fistulæ is not inconsiderable. Murchison (l. c., p. 501) mentions no less than eighty-six cases, and if we add those observations dating from a later period (especially from England) the number would easily exceed one hundred. With very few exceptions, such fistulæ are found in

[1] Case of Biliary Fistula communicating with the Lung: The Lancet, Dec. 13, 1879.

females of middle or advanced age. The fistulæ form in two ways. Either the ulcerative process, which starts from the gall-bladder or a dilated bile-duct, extends to the adherent abdominal walls, until the external skin finally ruptures, or the gall-bladder, or one of the bile-ducts, first experience an immoderate distention by the accumulation of bile and fluid inflammatory products, and then rupture externally, or they are opened with the knife under the erroneous impression that we have to deal with an abscess of the liver.

The position of the external opening of the fistula often corresponds to the fundus of the gall-bladder; it quite frequently penetrates the umbilicus, toward which the fistula may be led by the suspensory ligament of the liver (Murchison). The external opening of the fistula is sometimes found to the left of the median line of the abdomen, or in the inguinal region above the symphysis pubis, as in a case observed in Paris, in which two gall-stones were removed that had been imbedded in the subcutaneous cellular tissue in the vicinity of the clitoris. In rare instances two or more fistulous openings are present.

Bile, mucus, or pus in larger or smaller quantities, flow from these fistulæ, and calculi also usually escape from them. The number of gall-stones discharged in this manner has been found to amount, in individual cases, to several hundred, and in one case, indeed, to six hundred specimens. They sometimes have quite considerable dimensions. Fauconneau-Dufresne mentions a calculus which measured 3.15 inches in length, and 1.1 inch in thickness. The concretions sometimes appear immediately after the opening of the fistula, sometimes only after long duration of the latter, and even several years later. The fistula again closes after all the calculi have been removed from the cavity of the gall-bladder, but sometimes bile continues to flow through the fistulous opening for months after the discharge of the concretions. The fluid percolating from the opening is sometimes pure bile, the daily amount of which varies between very wide limits, viz., from about 200 to 2,000 c.c. But the bile may also be mixed with pus, mucus, or blood, or the fistula only secretes a very small quantity of purulent mucus. At the same time occlusion of the cystic duct is often present, in

which event the escape of bile will cease after the gall-bladder has been once emptied. When the biliary fistula is complicated with occlusion of the ductus choledochus, as has been observed in a few cases, the jaundice occasioned by the occlusion disappears, in great part, with the development of the former, although the fæces are, naturally, as destitute of biliary color as before. It more rarely occurs that the biliary excretory ducts are permeable, and that the bile flows externally through the fistula, and also into the duodenum by the natural way. After complete evacuation of the gall-bladder and discharge of all the gall-stones, the external opening of the fistula closes ; but the fistulous canal itself, which sometimes pursues a very sinuous course, and may present a considerable length, is obliterated into a fibrous cord, which connects the fundus of the gall-bladder with some point on the anterior abdominal walls. In sounding the fistula we quite frequently come in contact with calculi which are firmly imbedded in sac-like recesses of the fistulous canal, or the canal is entirely occluded by these calculi, so that the fluid must accumulate behind them, and may readily be the starting-point for the formation of new abscesses in the abdominal walls.

Finally, it has also been observed that gall-stones may pass through a fistulous opening in the abdominal walls, although no perforation is present in the biliary passages. The calculus, in such cases, has been retained in the intestines or vermiform appendix, and has finally given rise to a fistula, connecting the intestinal cavity with the external surface of the body. Siry observed a case of this kind in a woman æt. thirty years.

Diagnosis and Prognosis.

The diagnosis of the inflammatory changes in the abdominal walls which precede and prepare the way for the development of external biliary fistulæ, must depend chiefly on the previous history. If we have a patient who has notoriously suffered from attacks of cholelithiasis, or still suffers therefrom, if the preparatory inflammation assumes a slow course, if it is situated in the vicinity of the fundus of the gall-bladder, we will not go astray in the assumption that a biliary fistula is in process of forma-

tion. As soon as the fistula has penetrated the external skin, the diagnosis follows from the escape of bile and the discharge of gall-stones. If the latter are retained in the fistulous duct, exploration of the canal with the sound will almost always allow us to recognize their presence without any difficulty.

It cannot be denied, with regard to prognosis, that biliary fistulæ carry with them certain dangers to the patient, and that they must therefore always be regarded as a grave process, apart even from the long-continued disturbances and annoyances to which they give rise. But we must not forget, on the other hand, that biliary fistulæ constitute a mode of nature's healing of an extremely serious affection, viz., ulcerative cholecystitis, by which many patients attain complete recovery, while life is at least prolonged in others. Many patients affected with biliary fistulæ survive their development for a number of years, and enjoy good health ; in some cases the fistulæ heal entirely. There is more prospect of the latter occurrence when only one calculus, or a few, are present, when the external opening lies directly above the fundus of the gall-bladder, and the duct is presumably, therefore, very short, when, furthermore, no bile escapes, and jaundice does not exist, as occlusion of the cystic duct and permeability of the ductus choledochus are, therefore, demonstrated. On the other hand, the hope of permanent cure of the fistula is smaller when gall-stones have been left behind in the gall-bladder, or when the cystic duct is permeable, while the ductus choledochus is closed. In those fortunately rare cases in which the quantity of bile escaping through the opening is very considerable, rapid emaciation and prostration of the patient, general marasmus, and finally death may be the result of the biliary fistula. When many gall-stones are situated at the bottom of the canal, when the fistulous duct itself is long, very sinuous, surrounded by callous walls, while the external opening is very small, the affection may continue for years, inasmuch as an increase in the cicatrization of the fistulous opening occasionally becomes noticeable, but calculi then again escape, which must dilate the canal, that has, in the meantime, become narrowed, and thus causes the patient the greatest annoyance, while he enjoys good health in the interval.

Treatment.

We can only speak of the treatment of biliary fistulæ with reference to the cutaneous varieties. In some cases these fistulæ undoubtedly pursue a very simple course, and disappear again on account of the simple repair of nature, but, in many cases, the interference of the physician proves not alone useful but also indispensable.

The question must first be presented whether the preparatory inflammation, which precedes the perforation, should be left to itself, or whether the abscess in process of formation should be opened. This question must be answered according to general therapeutical principles, although the proper allowance should be made for the circumstances attending the individual case. In general, surgical interference should be held in abeyance until we are certain that the abscess has advanced near to the skin. If there is reason to distrust the adhesion of the abdominal walls to the gall-bladder, the use of caustics is indicated. On the other hand, if the skin is red, prominent, distinct fluctuation is present, and the pain and fever are very severe, we should proceed to open the abscess with the aid of the knife.

After the rupture of the inflammatory swelling has occurred, especially when gall-stones do not immediately appear in the opening, it is well to desist from any thorough examination for a few days until the fistulous canal and its external opening have become better defined. We may then enter with the catheter, search for the stones and remove them, by dilating the canal, according to circumstances, with laminaria and similar dilating substances, and endeavoring to aid the evacuation of the cavity by injections of luke-warm water.

The examination of the fistulous duct as well as all other surgical manipulations upon it must always be performed with the greatest care and delicacy, if we have to deal with fistulæ of long duration. The adhesions present may tear under rough and violent measures, so that general peritonitis with a fatal termination develops. It is not within our province to describe the technical details of the operation; we therefore refer to the handbooks on surgery.

So long as we are not convinced that all the gall-stones previously present have been removed, and the bottom of the fistula, therefore, entirely cleaned, it is advisable to keep the latter open, but if we have attained this conviction, the fistula may be left to itself. When pure bile flows from the opening in large quantities but none passes into the intestines, there is little chance of the closure of the fistula, and this is not desirable in such cases, for reasons readily understood. But if the ductus choledochus is permeable and the patient suffers from the exhaustion caused by the escape of bile through the opening, the question with regard to the closure of the latter must be taken into earnest consideration. The choice of measures, which may serve this purpose, must be left to the inventive spirit of the physician.

Parasites of the Biliary Passages.[1]

Among the list of animal parasites peculiar to man, the liver-fluke, round-worm, and echinococcus have been found in the biliary passages. But it can probably only be said of the distoma or liver-fluke that it has its regular and permanent seat in these organs. The round-worms, on the other hand, which are occasionally found in these canals, have wandered thither from the intestines, in which they normally stop. Finally, the relations of the echinococcus to the biliary passages are of various kinds. As a rule, the gall-ducts only form for a short time a passage for the echinococcus vesicles and through these they travel from an hepatic cyst, in which they were originally contained, into the intestinal canal. In rare cases, however, the echinococcus vesicles appear to develop from the beginning within the biliary passages, especially the gall-bladder, and there make a permanent stay. The multilocular echinococcus first infiltrates the walls of the large bile-ducts and the gall-bladder, inasmuch as it passes from the substance of the liver to the latter per continuitatem, but, at a later period, the small

[1] *Vide* the parasitic diseases in the third volume of this handbook, especially with reference to multilocular echinococcus of the liver and biliary passages.

folded vesicles may lie free in the cavities, especially the bile-ducts. With regard to psorospermia we refer to the close of the section on "Parasites of the Liver" in this volume.

1. Distoma hepaticum and Distoma lanceolatum.

Liver Leeches.

Davaine, Traité des Entozoaires. 2 éd. Paris, 1877, p. 253 (with the complete literature up to that time).—*Leuckart*, Die menschlichen Parasiten. I. 1863, pp. 530–610, and II., 1876, p. 868 et seq.—*Klebs*, Handb. d. pathol. Anat. I. Berlin, 1869, p. 519.—*Albers*, Atlas d. pathol. Anat. IV. Taf. XLV. (*vide* Erläuterungen zu dem Atlas IV. 1. p. 57).—*Biermer*, Schweiz. Ztschr. f. Heilk. II. 1863, p. 381.—*McConnell*, Remarks on the Anatomy and Pathological Relations of a New Species of Liver-fluke. The Lancet, 1875, Aug. 21, p. 271.

Liver-flukes, which are found so frequently and in such large numbers in the bile-ducts of the sheep and cow, and here produce severe anatomical changes with the symptomatology of the so-called cachexia aquosa, liver gangrene, or fluke disease, and often give rise to epidemic mortality in entire flocks, have been observed in very rare cases in the body of man. The literature of liver-flukes in man (*vide* Davaine, l. c.) comprises about twenty cases. The biliary passages, the gall-bladder as well as the larger and smaller ducts, form the regular abiding-place of the liver-fluke, but they have also been seen in other places, in the intestines, portal vein, the cellular tissue under the integument, etc. As opposed to the occurrence of these worms in the sheep, it must be stated, with regard to man, that the number of distomata found in the biliary passages is usually very small, and that only in few cases, and then only in very slight grade, do they give rise to anatomical changes in the affected organs. Hardly more than 4 or 5 cases have been known in which a large number of these parasites were present, in which they had caused decided anatomical lesions, and in which their presence had been revealed by a series of symptoms during life. These distomata, therefore, present quite a subordinate significance with regard to the human species.

The large liver-fluke (distoma hepaticum) is a sucking worm of a flattened, leaf-shaped appearance, the body anteriorly being

short (from 4 to 5 mm.), thick, nine-pin-like. In the mature state the worm attains a length of from 25 to 30 mm., and a greatest breadth (corresponding to the anterior third of the body) of from 8 to 12 mm. The animal is usually of a dirty brownish color, which is due to the yellow, brown, or blackish pigmented ova; the entire surface of the body is covered with small scales or spikes. At the tip of the conical anterior portion of the body is found the cephalic sucking-disk, at the base of the former and near the latter, the abdominal sucking-disk; midway between both is the genital opening. The liver-fluke is an hermaphrodite. Its mature eggs, which are laid in large numbers, possess a length of from 0.13 to 0.14 mm., and a width of from 0.075 to 0.09 mm. Their flattened anterior pole is provided with a cover, which opens and permits the embryo to escape.

The small liver-fluke (distoma lanceolatum) has a thin, elongated body which measures 8 or 9 mm. in length, and has a lancet-shaped figure. Its greatest breadth of 2 or 2.4 mm. corresponds to the posterior third of the body. Both sucking-disks are situated at a distance of one-fifth the entire length of the body from one another. The surface of this species is smooth, without spikes or scales. Like the large liver-fluke, it is also provided with both male and female genital organs. Its ova are from 0.04 to 0.45 mm. long and 0.03 mm. wide. With the aid of feeble magnifying powers we can distinguish in the quite transparent body of this worm, as well as of the distoma hepaticum, the ovaries branching like deer's antlers, and filled with brownish, pigmented ova, which occupy the entire posterior part of the body, and also the milky-white testicles in the vicinity of the lateral borders of the posterior part of the body, the intestines running out into two branches, and other organs.

The distoma hepaticum inhabits by preference the gall-bladder and the larger bile-ducts, while the distoma lanceolatum crawls into the narrow hepatic duct. Both species may infest the same individual, in man as well as in the sheep. On account of their small number[1] and size, their transparency and brownish

[1] *Buchholz* found a large number of worms of this kind in the gall-bladder of a criminal who had died of putrid fever. Leuckhart afterward decided that they were distomata lanceolata. In the body of a scorbutic individual *Brera* found the large hard

appearance, which has been not inaptly likened to withered foliage when soggy from rain, they may be easily overlooked while floating in the bile.

As early as the seventeenth century a few physicians mention the occurrence of distomata in the human liver. We are indebted to Pallas (1760) for the first positive observation. The majority of the reports hitherto known contain merely the statement that one or a few liver-flukes were found accidentally in the autopsy of this or that individual. We will not reproduce these observations, but refer to Davaine. Those cases, on the other hand, in which a larger number of distomata were found in the biliary passages, and in which morbid symptoms were observed during life, to which these parasites may be considered as standing in a causal relation, may be briefly collated, as follows :

1. In Milan, 1782, P. Frank saw a girl, æt. eighteen years, in a condition of extreme marasmus, the features cadaverous, the abdomen prominent, the pulse frequent and weak. The patient had suffered for six months from exhausting diarrhœa and pains in the region of the liver. On a few occasions the pains appeared in severe paroxysms. Jaundice had never been observed. Death occurred in convulsions. Autopsy : the hepatic duct had a circumference as large as a medium-sized quill. At its origin it formed a pocket, in which five live, greenish yellow, smooth worms were found as large as a silk-worm. (Davaine thinks that these should be considered distomata hepatica.)

2. Biermer (l. c. and in Leuckhart) reports concerning a soldier who was sent back from Sumatra to Europe while suffering from rapidly increasing jaundice. At the Zurich Clinic he presented an extreme grade of icterus, was very emaciated, but free from fever and pain. The liver not enlarged. Hepatic pains developed at a later period, then parotitis, scorbutic symptoms, finally, pneumonia and death. Autopsy : adhesive perihepatitis and complete occlusion of the hepatic duct at its bifurcation. Both conditions were regarded as the consequence of a distomata hepaticum, which Biermer found in the ductus choledochus. The bile-ducts were markedly distended, and, like the gall-bladder, filled with inspissated bile.[1]

3. The case observed by Kirchner and reported to Leuckhart is of exceeding

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liver "infiltrated with flukes and filled with distomata in its inner substance," sometimes singly, sometimes in groups containing a larger or smaller number (*vide* Davaine, l. c.).

[1] *Vide Klebs* (l. c.), p. 521, who—and apparently with justice—expresses doubt concerning the above-mentioned connection of the occlusion of the bile-duct with the presence of the liver-fluke.

interest: A girl, æt. fourteen years, the daughter of the village shepherd of Kaplitz, in Bohemia, was intrusted, since her ninth year, with the care of the sheep in a marshy district. She drank the water and ate the water-cresses (!) of this district. She had been sickly for a long time: the abdomen swollen, the thighs emaciated, loss of energy. Patient remained in bed six months until her death. The physician only saw her three days before, and noticed: œdema of the feet, considerable enlargement of the liver, acute pains in the hepatic region, which are said to have been present for several years. Autopsy: liver very large, and weighing eleven pounds; it contained eight gall-stones. Forty-seven perfectly developed specimens of distoma lanceolatum were found in the gall-bladder, which was strongly contracted and almost empty. It remained undecided whether there was any causal relation between the presence of the gall-stones and the distomata, nor were any definite data present to decide whether the abnormal condition of the liver was due to the parasites. Leuckhart remarks that it is not improbable that other distomata were concealed in the bile-ducts of the liver, which were overlooked at the autopsy.

4. A Chinese carpenter,[1] æt. twenty years, who is said to have suffered for several weeks from severe fever, and was brought into the Calcutta Hospital in a moribund condition, died there after a few hours. The autopsy showed a severe hepatic affection with its sequences (cholæmia, anæmia), these changes being attributable to parasitism of liver-flukes. The hepatic ducts were filled and made impermeable by fifty to sixty of these worms. From the description of these worms given by McConnell (The Lancet, Aug. 21, 1875), they present a greater similarity to distoma lanceolatum than distoma hepaticum. Leuckhart conjectures in them a new species which he terms, for the present, distoma spathulatum.

A survey of the entire literature[2] of the parasites in question furnishes the noteworthy conclusion, as Klebs had already pointed out, that the distoma hepaticum appears to produce much less damage in man than the distoma lanceolatum, which is probably due to the fact that the latter is usually found in much greater number than the former. While among eleven cases of distoma hepaticum diseases of the biliary passages were

[1] *Leuckhart*, Parasiten, II., p. 871.

[2] These eight cases are increased to eleven if I add *P. Frank's* case, which was excluded by *Klebs*, also the recent case of *Wyss* (Arch. d. Heilk., IX., 1868, p. 172), and, finally, *Murchison's* observation (Diseases of the Liver, 2 ed., p. 634). The literature of distomata has received a still further increase in *Prunac's* observation (Gaz. des hôp., 1878, No. 144, 12 Dec.): a woman, æt. thirty-one years, suffering from severe symptoms indicative of a gastric ulcer, after taking a laxative, passed more than thirty specimens of distoma hepaticum, in addition to round-worms and a tænia. The hepatic region was continually painful.

produced, at the most, in two, among three cases of distoma lanceolatum notable changes of the liver and bile-ducts were twice combined with the parasitism of these worms, and in only one case is no mention made of such changes.

The *etiology* of the distoma disease is not yet sufficiently clear, as gaps are still found in the embryological history of these worms. According to Leuckhart's conjecture, the ingestion of liver-flukes (in their immature form, the cercariæ) occurs by means of certain small, thin-walled snails which are accidentally swallowed with the fodder. The snails infested by the cercariæ could as readily enter with the drinking water, badly cleaned salad, water-cresses, etc., into the stomach of man, in which the young distomata are set free, and find an opportunity for further development. In addition to other noteworthy circumstances, this conjecture also agrees with the fact that liver-flukes have been hitherto especially found in people belonging to the poorer classes, who would be most likely to obtain food and drink of the character referred to. According to Biermer, residence in southern countries will increase the danger of the ingestion of distomata.

The anatomo-pathological changes produced by distomata in large numbers consist of a chronic cholangitis, with considerable fibrous thickening of the walls of the bile-ducts and separation of a mucoid or purulent secretion at the surface of the mucous membrane, which accumulates in the canals and dilates them. As has been previously stated, these changes rarely appear to reach any notable severity in man. When few distomata are present, the bile-ducts, as a rule, were found intact. The distomata can probably not produce direct occlusion of the bile-ducts, but it is possible that they may indirectly, by means of the cholangitis, lead to closure of the excretory duct, as occurred in Biermer's case.

The symptoms[1] of the distoma disease are very variable. They are partly of a subjective character, and consist of dull sensations of pain in the hepatic region. The objective symptoms refer sometimes to the liver (enlargement, symptoms of

[1] *Vide Prunac*, De la douve chez l'homme, Gaz. des hôp., 1878, No. 144.

biliary retention), sometimes to the stomach and intestinal canal (disturbances of digestion, hæmatemesis, bloody stools), sometimes, finally, to nervous symptoms (syncopal attacks, aphonia, convulsions, etc.). In time the entire economy suffers ; emaciation, failing of the powers progressing to complete exhaustion, dropsy, and, finally, death occur.

The diagnosis will not pass beyond the region of surmise until distomata have been evacuated in the passages or vomit. As mature distomata leave a large number of ova in the biliary passages (Leuckhart), and these are presumably washed into the intestines with the bile, we must pay attention to the presence of the ova of these parasites (*vide* above) in the fæces in cases in which there is reason to suspect the distoma disease, and subject the stools to a microscopic examination.

If we should ever be placed in a position in which we are required to give a prognosis, it should be declared favorable, as there is a possibility of removing the parasites from the biliary passages. An unfavorable exception would then occur when occlusion of the biliary excretory duct is present at the same time.

It goes without saying that there can only be a question of treating the distoma disease, when the diagnosis is rendered positive by the passage of the worms themselves, or of their ova. We should then rely upon the use of anthelmintics, saline cathartics, and the alkaline saline mineral-waters (Carlsbad, Vichy, Ems, etc.). Special attention should also be devoted to the general nutritive condition. With regard to prophylaxis, we should advise abstinence from the use of suspicious drinking water, and caution in eating fresh vegetables in the form of salad, etc.

2. Ascaris lumbricoides.

Round-Worm.

Davaine, Traité des entozoaires. 2 éd. Paris, 1877, p. 157 (with the histories of 37 cases. Special attention has been paid to the older cases).—*Leuckhart*, Die menschlichen Parasiten. II. 1876, pp. 236–240 (with mention of other cases in recent times).—*Bonfils*, Des lésions et des phénomènes pathologiques

déterminés pars la présence des vers Ascarides lumbricoides dans les canaux biliaires. Arch. gén. de méd. June, 1858, p. 661.—*Lebert*, Traité d'anat. patholog. Paris, 1871. I., p. 412, and Atlas. I., pl. LXI., Fig. 1.—*Frerichs*, Klinik d. Leberkrankhtn. II., p. 457.—*Klebs*, Handb. d. pathol. Anat. I. 1869, p. 523.—*Vinay*, Observat. d'ictère généralisé tenant à la presence des lombries dans les voies biliaires. Lyon méd. 1869, I., p. 251.—*Scheuthauer*, Kaesig zerfallende Herde in der Leber, bewirkt durch Spulwuermer in den Gallengaengen. Jahrb. d. Kinderheilk. N. F. XIII. 1878, p. 63.

At the present time it may be regarded as settled that round-worms which are found in the biliary passages have not developed there, but have emigrated from the intestinal canal in every case, and have wandered into the biliary ducts. Observations of this kind have been made in former and in recent times. Davaine mentions thirty-seven cases;[1] Leuckhart makes a low estimate of those published until 1877 as forty odd cases. The literature of the last few years also includes a number of observations belonging to this category. These numbers appear small when compared with the very frequent presence of ascarides in the human intestines. But I am convinced that the pathological anatomist by no means regards the presence of round-worms in the biliary passages as a rare occurrence. I myself have found them in this locality six times in a very moderate number of autopsies, and my colleagues have probably had a similar experience.

As a rule, we only find one or a few round-worms, often still alive though benumbed with the cold, in the entirely unchanged biliary passages, and may, therefore, justly conclude that the worms have only entered these canals shortly before death, or, perhaps, even after its occurrence. Sometimes, however, they remain here for a long time, and then give rise to deep-seated, anatomical changes in the biliary passages and liver, produce the most severe symptoms, and may even be the cause of death.

That the round-worms usually enter the ductus choledochus in the natural way, through the porus biliarius, is evident from several observations in which, although the organs in question were perfectly intact, a worm was found with the anterior extremity in the ductus choledochus and the other end sticking in

[1] Two cases follow in the Appendix, p. 933, making thirty-nine in all.

the duodenum.[1] The worms are always found with the cephalic extremity directed forward in the biliary passages unless they have turned around in the gall-bladder or in sacculated dilatations of the ducts, and the cephalic end has again approached the porus biliarius. The size, and especially the thickness, of the round-worms evidently form no serious obstacle to their entrance into the narrow porus biliarius. It must be considered that the worms have possibly only attained the size, which they present at the autopsy, during their stay in the biliary canals, and also that those which have been found in the bile-ducts were usually small.

With the notorious predilection of ascarides for forcing themselves through narrow openings,[2] they will scarcely, with their slender, wedge-shaped body, which gradually increases in thickness, find an insurmountable obstacle in the narrow duodenal end of the biliary excretory duct, as that opening is so yielding and dilatable that it can also be passed by gall-stones of not inconsiderable dimensions, although the external conditions are much more unfavorable in the latter case. There is, therefore, no reason for accepting Davaine's opinion that the bile-ducts, and especially their mouth, the porus biliarius, must be abnormally dilated by preceding pathological processes (passage of gall-stones or echinococcus vesicles), in order that the ascarides can succeed in effecting an entrance. Davaine's assumption would especially not hold good in children, in whom ascarides have been most frequently observed in the biliary passages.

Exceptionally, the round-worms enter the biliary canals in pathological ways, viz., when abnormal communications have formed between the inside of the gall-ducts and the intestinal cavity by means of inflammatory and ulcerative processes. In a case recently published by Goeller[3] I saw, in an old man, a softening spot form from cheesy lymphatic glands in the neighborhood of the duodenum, and which had ruptured into the in-

[1] In Pellizzari's case (quoted by *Leuckart* and *Davaine*, p. 933) six well-developed female ascarides were found with half their bodies enclosed in the ductus choledochus, while the remainder was in the duodenum. The narrow porus biliarius (two mm.) must therefore have been dilated to a diameter of at least two ctm.

[2] *Vide Leuckart*, l. c. II., p. 236.

[3] Dissert. aug. Tübingen, 1879.

testines and hepatic duct as well as into the portal vein. Several round-worms had then passed from the duodenum through the cavity of the abscess partly into the bile-ducts, partly into the branches of the portal vein. Whether this occurred before or after the death of the patient must remain undecided.

We do not venture to give a positive answer to the practically not unimportant question, whether ascarides, which have already penetrated the gall-duct, can again return to the intestinal canal through the natural channel. Many physicians affirm either expressly, or at least, tacitly, the possibility of such a return, but they rely partly upon deceptive premises. When, for instance, a patient becomes icteric because the ductus choledochus is occluded by a round-worm, we may not necessarily conclude from the later disappearance of the jaundice, even when ascarides are passed at the same time from the intestines, that the round-worm in question has left the ductus choledochus and crawled back into the intestine. It would only be necessary for the worm to enter the gall-bladder or pass still farther into the hepatic duct, in order to effect the same object, viz., the rapid disappearance of the jaundice. Others, on the contrary, deny that the worm has the power of crawling backward, *i.e.*, with the tail end foremost, from the gall-ducts into the intestines, and only admit the possibility of its return under the supposition that it has previously turned around, either within the gall-bladder or in a sacculated dilated portion of the bile-duct.

The number of ascarides found in the biliary passages in any individual may vary very considerably. Usually only one or a few (three to four) have entered; their number is rarely much larger. Pellizzari[1] found in one patient sixteen ascarides, which were situated partly in the gall-bladder and excretory ducts, but partly, also, deep in the liver. Murchison[2] saw a specimen in the Vienna General Hospital in which the ductus choledochus was converted into a sac as large as a man's fist, and was filled with a large number of round-worms. The worms are often found alive, perhaps only torpid; in other cases they are dead, and we can conclude, at times, from the soft and macerated con-

[1] Quoted by *Leuckart*, l. c., p. 238.

[2] Clinical Lectures, 2d ed. p., 345.

dition in which they are found, that their death occurred a long time previously. Dead and macerated ascarides are especially found in the hepatic abscesses to which they have given rise.

The anatomo-pathological changes, which are produced by the ascarides that have entered the biliary passages, are of a very severe character. In the first place, they give rise to occlusion of the biliary excretory duct, in consequence of which retention of bile and dilatation of the biliary passages are produced. We leave it undecided whether the dilatation can attain such a height, that this alone can cause rupture of the canal, as Davaine maintains and which he thinks is proven by some cases which he adduces. The connection accepted by Davaine is not probable, but rupture of the canal may, perhaps, occur when it has been previously prepared for such an event by ulcerative processes incited by the parasites. The dilatation of the biliary passages is at times locally circumscribed and sacculated; the walls of the sac, in which the worms lie rolled up, are sometimes smooth, or they present the signs of intense inflammation, or even an irregular nodular surface which is in a condition of ulcerative degeneration. When round-worms are present in the biliary canals for a long time they always produce intense cholangitis by which the walls of the ducts are swollen and thickened, their cavities filled with pus, and the mucous membrane appears covered with ulcers. The inflammation is sometimes more circumscribed, but sometimes very extensive and not by any means confined to those canals which are directly inhabited by the worms. Furthermore, the purulent cholangitis often extends, especially in children, to the adjacent hepatic tissue and purulent softening spots or true circumscribed hepatic abscesses develop. These are scattered throughout various portions of the liver, sometimes attain a considerable size, are on the average about as large as a walnut, and are usually in evident communication with the lumen of the biliary passages. In exceptional cases a communication of the abscess with the bile-ducts cannot be detected. In the case described by Lebert (l. c.) of a factory girl, æt. fifteen years, one of the hepatic abscesses perforated the diaphragm, right lung, and bronchus, and the other severe disturbances were reinforced by a pneumo-thorax on the right side,

after which the patient rapidly succumbed to her sufferings. Kirkland[1] saw a round-worm appear, in addition to pus, from an hepatic abscess which had ruptured externally.

Scheuthauer (l. c.) found in the right branch of the hepatic duct of a child æt. four years, two fresh female round-worms whose heads were directed toward spots as large as a walnut and hazel-nut respectively. Four similar spots were found which were free of worms, but contained numerous mature non-segmented ascarides ova. All these spots consisted of numerous dilated bile-ducts, as large as straws, with walls one-half mm. thick and, instead of the hepatic parenchyma, of tough, grayish white nodules or, more frequently, of cavities as large as a pea and filled with a crumbling cheesy mass or a tubercle-like pap. These cavities, hitherto termed abscesses, are not, according to Scheuthauer, true abscesses, but, as was shown by the microscopical examination, foci (?) which have undergone cheesy degeneration on account of the excessive accumulation of small round cells, which have been produced by the long-continued presence of live ascarides. The presence of the ova proves that these parts were inhabited by ascarides. As a perforation of the surface of the liver was not present and the cavities were too small to permit the worms to turn, it is to be presumed that the parasites returned to the intestine by a retrograde movement from the peripheral bile-ducts.

The symptoms produced by ascarides, which have penetrated the biliary passages, are very manifold in character. The symptomatology, in a concrete case, is often complicated by the fact that a large number of round-worms are present in the intestines, where they give rise to all kinds of abnormal manifestations, especially in delicate and irritable individuals, such as children. Often, indeed, all symptoms of an affection of the liver are absent although round-worms are present in the biliary passages, but only when they are merely present in the canals for a short time, and perhaps have only entered them after the death of the patient.

The most important symptom is jaundice, which results from the distention of the ductus choledochus by the body of the round-worm. The jaundice disappears as soon as the worm crawls forward into the gall-bladder or into the hepatic ducts, and the excretory duct is again permeable to the bile. The entrance and advance of the worm may occur so rapidly that icte-

[1] An Inquiry into the Present State of Medical Surgery. London, 1786.

rus does not occur at all, because the occlusion of the ductus choledochus is so brief. It must not be forgotten that the icterus may merely be symptomatic of a duodenal catarrh which has extended to the ductus choledochus and which will hardly ever be absent when large numbers of ascarides are accumulated in the duodenum. This also holds good with regard to the enlargement of the liver and gall-bladder, so far as these signs are the expression of retention of bile; all these symptoms are peculiar to duodenal catarrh as well as to occlusion of the ductus choledochus by ascarides.

The inflammatory changes in the biliary passages and liver, which occur after a long stay of the round-worms in these parts, are manifested by severe pains in the right hypochondrium and epigastrium, which are increased by pressure upon the hepatic region or by vigorous movements of the body. The liver is then very considerably enlarged even though icterus is not present. If purulent hepatitis occurs, all the local and general symptoms of hepatic abscess develop, especially intense fever with frequently recurring chills, high temperature of the body, etc. The symptoms present, at the same time, on the part of the digestive tract, viz., anorexia, constipation or, on the contrary, continuous diarrhœa, emesis, passage of bloody masses in the stools, etc., should only be partly considered as the results of the ascarides present in the biliary passages, or of the hepatic affection produced by them. They are probably due in greater part to the accumulation of the round-worms in the intestines.

Finally, ascarides in the biliary canals, especially in children, produce severe nervous symptoms, such as attacks of syncope, vertigo, tinnitus aurium, but particularly convulsions. The latter must be regarded as reflex spasms, the starting-point of which is the irritation of the hepatic plexus. Moreover, these nervous symptoms, at least in part, may also be attributed to the disturbance of the entire organism, above all, to the general anæmia caused by the helminthiasis.

It cannot be disputed that all the symptoms mentioned are insufficient to furnish a positive diagnosis of ascarides in the biliary passages. In a concrete case we can only venture a conjecture, be it ever so probable.

The duration of the disease may be short, and all the symptoms, especially the jaundice, may disappear after a few days. As soon, however, as deep-seated changes have occurred in the liver, the disease progresses in a rather uniform manner until the fatal termination, which generally appears within a few weeks or months. A fatal termination must be regarded as the rule in severe cases and in those in which hepatic abscesses have formed. But as it is not impossible, as we have seen, that the ascarides may return to the intestines, the termination in recovery is not by any means excluded. Even in the most serious case, that of purulent hepatitis, recovery is still possible by the rupture of the abscess and the expulsion from it of the ascarides, either externally through the skin (as was really observed by Kirkland) or into the intestinal canal.

On account of the uncertainty of the diagnosis, the prognosis can only take into consideration the more important symptoms. So long as jaundice alone is present, the prognosis is good, but when this symptom continues for a long time it becomes daily more unfavorable. If the signs of hepatic abscess appear, if high fever is present, and the entire organism is seriously affected, the prognosis must be regarded as bad, and, indeed, almost fatal.

The treatment has for its object the removal of the round-worms, for which purpose santonin and the other ordinary anthelmintics are employed. The jaundice has several times been found to rapidly disappear after the evacuation of ascarides caused by these remedies, although, as a matter of course, this does not by any means prove that the worms have been removed from the biliary passages. It is indeed extremely questionable whether round-worms can be made to leave the biliary passages from the effect of anthelmintic remedies.

In other respects the treatment of the diseases in question is purely symptomatic.

3. Echinococcus.

Davaine, Traité des Entozoaires. 2 éd. 1877, pp. 481–501.—*Frerichs*, Klinik der Leberkrankhtn. II. S. 224.—*Musehold*, Ein Fall von Echinococcus der Gallenblase u. d. Leber. Diss. Berlin, 1876 (Vide *Virchow*, in Charité-Annalen. III. Jahrg. 1876. S. 766).

The relations of the echinococcus to the biliary passages are manifold in their character. Although echinococcus cysts occur so frequently in the liver, the hepatic bile-ducts are only affected in comparatively rare cases. Under the pressure of the hydatid sacs they may become impermeable and finally be obliterated. Leroux's case, published by Davaine (l. c., p. 476), is remarkable in this respect; the gall-bladder had disappeared in this manner and no traces could be found of the hepatic ducts, the ductus cysticus and choledochus.

Furthermore, the echinococcus sacs enter not very rarely into open communication with the lumen of the biliary passages. At times only one large bile-duct, at others a large number open into the cavity of the cysts. According to the general opinion this event is attended with bad effects upon the parasites, as it is thought that death of the echinococci, and inflammation, suppuration, and gangrene of the sac will be caused by the bile which, under such circumstances, comes in direct contact with the echinococcus vesicles. It will be shown later, that well-founded doubt may be entertained with regard to this view.

As soon as the communication of the hydatid sac with the bile-ducts has been established, the vesicles can pass out of the cyst into the lumen of these canals, dilate and occlude them, and give rise to inflammation and ulceration of their mucous membrane; or the vesicles gradually pass through the ducts, and finally reach the intestines through the ductus choledochus, after which they are discharged externally without further disturbance. The passage of echinococcus vesicles through the biliary excretory ducts produces exactly the same symptoms (hepatic colic) as the difficult passage of gall-stones. In many cases an examination of the stools can alone decide whether an

attack of colic of this kind was due to the passage of gall-stones or of echinococcus vesicles. Complete discharge and cure of the hydatid sacs in this manner is a rare occurrence; the process usually runs an unfavorable course, either because the ductus choledochus is permanently occluded by the vesicles and fatal jaundice develops, or suppuration and gangrene of the sac, or inflammation and ulceration of the bile-ducts and the adjacent parenchyma of the liver supervene. The case described by Bahrdt (Arch. d. Heilk. 1872, p. 467) may serve as an example of complete recovery in the manner here described. When the hydatid sac, as has been observed on several occasions, opens into the gall-bladder, evacuation of the sac may also follow, inasmuch as the echinococcus vesicles are carried through the ductus cysticus and choledochus into the intestines.

With regard to the part taken by the biliary passages in multilocular echinococcus tumors, we refer to the corresponding section in Volume III. of this cyclopædia. Icterus is more frequently present than absent in this disease, *i.e.*, the large bile-ducts in the transverse fissure of the liver are, in the majority of cases, affected by the multilocular echinococcus. In addition to the larger branches of the hepatic duct, the trunk itself, together with the adjacent part of the ductus choledochus, the ductus cysticus, and a large portion of the wall of the gall-bladder, are not infrequently implicated in the degeneration. The walls of the ducts and of the gall-bladder are converted into a rigid, unyielding, very hard mass by the numerous echinococcus vesicles (often hardly as large as the head of a pin or a grain of sand) imbedded in them; they appear markedly thickened, and the lumen of the ducts has disappeared, or is filled with a number of folded, small vesicles. The infiltrated portions of the biliary passages may also take part in the later ulcerative destruction, and this is especially true of the gall-bladder. The ulceration usually occurs independently of the softening and cavernous formation within the hepatic tumor, but it begins rather on the surface of the mucous membrane, which is infiltrated like a sieve with the smallest parasitic vesicles, and thence spreads to the deeper layers of the walls of the canal. In this manner small, irregularly shaped cavities, surrounded by hard walls, form in the transverse

fissure of the liver, and their connection with the biliary excretory ducts is readily recognized with a little attention.

Of predominant interest is the question, whether the echinococcus may remain permanently in the biliary passages, develop here, and, on the whole, continue to exist. As is well known, it is almost universally maintained (chiefly upon the authority of Davaine) that this is not the case. Everything indicates, says Davaine, that the echinococcus never develops in cavities lined with a mucous membrane, and, in addition, the echinococcus vesicles, which are surrounded by bile, would be soon killed and destroyed by the latter. The notion of some physicians that an echinococcus sac, which is in open communication with a bile-duct, has originally developed in this canal, must, indeed, be discarded as unfounded, and in general the statement holds good that echinococcus vesicles, which are found in the biliary passages, have only entered the lumen of the latter secondarily by means of perforation, in the same manner that they may reach the bronchi or intestines by perforation from an hepatic cyst. However, several observations have been made in recent times, from which it would appear that the echinococcus may primarily develop (although in rare cases) in the biliary passages, and may exist and develop as readily in them as in an ordinary echinococcus sac of the liver.

Musehold [1] reports the case of a laborer, æt. thirty-one years, whose liver contained an echinococcus sac, which was entirely closed. In addition, however, the gall-bladder, which was transformed into a cyst fully as large as an apple, with thick fibrous walls, contained six echinococcus vesicles as large as cherries, and a number of smaller ones. These vesicles were bathed in bile on all sides. The cystic duct was also involved in the dilatation of the gall-bladder. The bile found free vent from the intra-hepatic canals into the gall-bladder, which was filled with the naked vesicles of the parasite; the ductus choledochus, on the other hand, was closed by a tense, healthy echinococcus vesicle as large as a cherry, which projected from the transverse fissure of the liver into the first part of the ductus choledochus. In this manner the bile was prevented from flowing into the intestine, and icterus necessarily developed. There was no trace of any communication of the echinococcus sac, which was imbedded in the substance of the liver, with the dilated biliary passages. For this reason, and because all the worms in

[1] Dissert. inaug. Berlin, 1876. This case is probably identical with that referred to by Virchow (Charité-Annalen, III. Yahrg. 1876, S. 766).

the gall-bladder, etc., were well preserved, no interpretation remains but that the echinococci in this patient must have developed, from the beginning, within the cavity of the gall-bladder; hence follows the further consequence that the hitherto prevalent idea concerning the deleterious influence of the bile upon the parasitic vesicles must be renounced as untenable.

Perhaps the following case, reported by Dickinson (Trans. of the Path. Society, Vol. XIII., 1862, p. 104), belongs to the same category.

A girl, æt. sixteen years, affected with purpura and deep jaundice. Liver soft, dark olive-green. The gall-bladder contains but little bile, and is distorted by a round tumor as large as a ball. This tumor is an hydatid sac, with numerous small daughter-vesicles; the cyst appears to have started from the dilated right branch of the hepatic duct, its wall is thick and rigid, lined by the dark-colored mother-vesicle, which is ruptured, so that the daughter-vesicles are floating free in the sac. A large piece of the mother-vesicle had passed into the chief branch of the hepatic duct, and, together with inspissated bile, formed a plug by which the canal was distended. The plug projected even into the ductus choledochus. The cystic duct was patent. The mother-vesicle had, therefore, probably developed originally in the right branch of the hepatic duct. Duration of the jaundice, six weeks.

Gall-Stones.—Cholelithiasis.

(*Hepatic colic, Gall-stone colic—Colica hepatica.*)

Conr. Gessner, De omni rerum fossilium genere. Turici, 1565.—*Fernelius*, De morbis univers. et particul. Lugd. Bat., 1645. T. II. p. 251.—*Glisson*, Anatomia hepatis. London, 1654.—*Bianchi*, Historia hepatica, etc. Turin, 1710.—*Friedr. Hoffmann*, Medicin. ration. system. T. VI. Halae, 1737. (De dolore et spasmo e calculo felleo.)—*Morgagni*, De sedibus et causis morbor. 1762. Epist. 37. (De ictero et de calcul. biliariis.)—*A. v. Haller*, Elementa physiol. corp. hum. Lausanne, 1757–1766. (lib. XXIII. Hepar et bilis.)—*J. F. Durande*, Observat. sur l'éther sulfurique et l'huile de terebinth. dans les coliques hépat. Dijon, 1774 and 1782. (Id., Thèse de Montpellier, 1784.)—*Soemmering*, De concrement. biliar. corp. hum. Francof. a. O., 1795.—*Aug. Walter*, Museum anatomicum. I. Berlin, 1796.—*Prochaska*, Opera minor. anat. physiol. et pathol. T. H. Viennae, 1800. (De calculo felleo.)—*Pujol*, Œuvres de méd. prat. Paris, 1802.—*Portal*, Observat. sur la nature et le traitement des maladies du foie. Paris, 1813.—*Flemming*, Ein Beitrag zur genauern Diagnose

grösserer in den Gallenwegen eingeklemmter Gallensteine. Leipzig, 1832.—*Andral*, Clinique médicale. 3. édit. Paris, 1834. T. II.—*Cruveilhier*, Anat. pathologique, mit Atlas (livr. 12, pl. 5, and livr. 29, pl. 4).—*Bouisson*, De la bile, etc. Montpellier, 1843.—*George Budd*, On Diseases of the Liver. London, 1845. (German by *Henoch*. Berlin, 1846.)—*Hein*, Ueber Gallensteine als Krankheitserzeugnisse. Ztschr. f. rat. Med. IV. 1846. S. 293.—*Bramson*, Ueber Gallensteinbildung. Ztschr. f. rat. Med. IV. 1846. S. 193.—*Fauconneau-Dufresne*, La bile et ses maladies. Mémoir. de l'acad. roy. de médicine. 1847. XII. p. 36.—*Idem*, Traité de l'affection calculeuse du foie, etc. Paris, 1851.—*Idem*, Nouvelles observat. sur la colique hépat. Gaz. hébdom. 1859.—*Seifert*, Ueber Zusammensetzung u. Entstehung der Gallensteine, Ztschr. f. rat. Med. X. 1851. S. 123.—*Bamberger*, Krankhtn. d. chylopoët. Systems. (Virchow's Hdb. d. Path. u. Ther. VI. 1. Abth. Erlangen, 1855. S. 619.)—*H. Meckel*, Mikrogeologie. Ueber die Concremente im thier. Organismus. Edit. *Billroth*. Berlin, 1856.—*Henoch*, Klinik d. Unterleibskrankhtn. 2. Aufl. Berlin, 1856. II. Bd. S. 221.—*Lebert*, Traité d'anat. pathol., avec Atlas. Paris, 1857–1861. I. p. 369. Pl. LI. CXXIV. Fig. 9–11. CXXV. Fig. 6.—*Oppolzer*, Ztschr. d. Ges. d. Aerzte in Wien.—*Idem*, Wiener med. Wochenschr. 1866.—*Frerichs*, Klinik d. Leberkrankhtn. H. Braunschweig, 1861. M. Atlas.—*Willemin*, Des coliques hépatiques et de leur traitement par les eaux de Vichy. Paris, 1862. (2. éd. 1870.)—*Wolff*, Beiträge zur Symptomatologie u. Diagnostik d. Gallensteine. Virchow's Arch. f. path. Anat. XX. S. 1, 1861.—*Thudichum*, A Treatise on Gall-stones. London, 1863.—*Trousseau*, Clinique médicale de l'Hôtel-Dieu de Paris. T. III. 2. édit. 76. leçon. p. 213–235. 1865.—*Luton*, Du traitement de l'affect. calcul. du foie. Bulletin de thérapeut. Mars 15, 1866.—Dictionnaire encyclopéd. des scienc. méd. Réd. par *Dechambre*. T. IX. Paris, 1868. (Art. Voies biliaires von *Barth* u. *Ern. Besnier*, p. 384 ff.)—*Brodmann*, Ueber Gallensteine u. ihre Folgen. Diss. Berlin, 1868.—*Schwechten*, Ueber Cholelithiasis. Diss. Berlin, 1869.—*Ritter*, Recherches chimiques sur la composit. des calculs biliair. humains. Robin's Journ. de l'anat. et de la physiol. VIII. Année. 1872, p. 60.—*O. Wyss*, Ueber Gallensteinzertrümmerung. Betz' Memorabilien, 1873. No. 1.—*Murchison*, Clinical Lectures on the Diseases of the Liver. 2d edit. London, 1877, p. 482 ff.—*Charcot*, Leçons sur les maladies du foies et des reins, publiées par Bourneville et Sevestre. Paris, 1877.—*Alfred Fiedler*, Ueber Gallensteine. Jahresber. d. Gesellsch. f. Nat. u. Heilk. in Dresden, 1878–79.

Compare, furthermore, the Handbooks of Physiological and Pathological Chemistry of *Schwann*, *Hoppe-Seyler*, *Gorup-Besanez*, and others.

The reports of cases of gall-stones are exceedingly numerous. Among the many sources where they may be found, we will only mention two as especially rich, viz.: the Bulletin de la Soc. Anat. de Paris, and the Transactions of the Pathological Society of London.

History.

Cholelithiasis constitutes by far the most important affection among diseases of the biliary passages, both to the physician and the patient, as well on account of the frequency of its occurrence and the severity of its attacks as on account of the manifold sequels and dangers to which it gives rise. It has for a long time claimed the attention of physicians, and been the subject of most thorough study. Numerous methodical investigations, and the overwhelming abundance of reported cases, bear witness to the lively interest which physicians have at all times felt in this disease. But, despite the zeal with which the study of gall-stones has been pursued, there are still a good many points waiting to be cleared up. The discussion of this question, as we are about to pursue it, will reveal to us the strong and weak points in our knowledge of gall-stones, and of the disturbances dependent on them.

Marcellus Donatus (De medica historia, lib. IV. Mantuae, 1586) points out Gentilis von Foligno, in the fourteenth century, and Johann von Tornamira, Professor in Montpellier at the end of the fourteenth and beginning of the fifteenth century, as being the first who found gall-stones in the human body. Anton Benivieni, of Florence, comes very near to the latter in point of time. His work, "De abditis quibusdam ac mirandis morborum causis," gives two quite indefinite observations of gall-stones, viz., Observ. III., "Lapides in tunica hepatis reperti;" and Observ. XCIV., "Calculus in tunica fellis." Some more accurate observations of gall-stones were made by the Dresden physician, Jo. Kentmann, who communicated them to Conrad Gessner for his celebrated book on fossils (De omni rerum fossilium genere. Turici, 1565), and furnished pictures of the objects found. In the same century Fallopius, Vesal, and others described gall-stones quite fully, and in the seventeenth century these concretions were well known to all physicians, as may be seen, more particularly, from the book of Fernelius (see "Literature"). Some material, also, began to be contributed toward the study of the pathology of this affection. But it was not until the

eighteenth century that the pathology of gall-stones was thoroughly worked up, particularly by the celebrated Friedrich Hoffmann, in Halle, as well as shortly before and after him by Bianchi, Boerhave, van Swieten, Sydenham, Sauvages, and others. While Albrecht von Haller, in the middle of the previous century, had collected the observations made up to that time, it remained for Morgagni, in his work, "De sedibus et causis morborum," which marked an epoch in medicine, to give a critical and fully rounded description of cholelithiasis, from which the state of knowledge at his time is clearly to be recognized. The labors of the period following were, to a great degree, devoted to the investigation of the physical and chemical character of gall-stones. In this connection the names of Fr. Aug. Walter, Soemmering, Prochaska, and later, H. Meckel and others, are to be mentioned. Galeatti, as early as 1748, had occupied himself with the chemical composition of gall-stones, although his labors led to no satisfactory result. It was not until after Fourcray and Thénard had enriched science with the knowledge of cholesterine that we could look for practical results in that line. Among the large number of works on the chemical constitution of the bile and of gall-stones which have appeared in more recent and most recent times, we give special prominence to those of Bramson, Hein, Seifert, Bouisson; later, to those of Strecker and Thudichum, and finally to those of Jacobson and Ritter, because these men have adhered to the question of the origin of the concretions and their cause—in fact, to the medical side of the question generally. The pathology, the symptomatology and diagnosis, as well as the therapeutics of cholelithiasis, have been materially enriched in almost every decade of this century, and have been discussed by numerous authors in a more or less comprehensive manner. Among many others the contributions of Andral, Trousseau, Frerichs, and Murchison may be mentioned as being of special value, and as, in part, marking an epoch in the literature of this subject.

In the year 1851, cholelithiasis was made the subject of a monograph by Fauconneau-Dufresne, which, aside from other advantages, is especially valuable, because it reproduces, in extenso, numerous observations and reports of cases by other

authors. It is to be regretted, however, that the author gave somewhat undue prominence to the French literature of the subject, while foreign, and especially German works, were only used by him to a limited extent.

Physical Characteristics of Gall-Stones.

Gall-stones result from the precipitation of certain substances held in solution in the bile, the amorphous or crystalline precipitate uniting to form larger or smaller concretions. The formation of these concretions takes place chiefly in the gall-bladder. Here they are usually to be found in certain numbers—as a rule, about five or ten at a time. Their number is extremely variable, and the average figures given above are often enough greatly exceeded, a hundred or several hundred stones of the average size of a pea being found in the gall-bladder at once.

In rare instances the number of calculi found in the gall-bladder is astounding. Thus Frerichs counted 1,950 in a woman sixty-one years old; Dunlop,[1] 2,011 in a woman ninety-four years old; Morgagni, 3,000; Hoffmann, 3,646; Otto, 7,802 in one gall-bladder. When a large number of gall-stones are found in one person, they usually all show the same characteristics; they are alike in their external appearance, in their size, structure, and chemical composition. It is only exceptionally that one stone differs from the rest in its physico-chemical relations. According to Hein,[2] this occurred twenty-eight times in 632 cases (4.43 per cent.). Sometimes but a single stone is found in the bladder, and it is then generally very large, so that it sometimes completely fills the organ, and represents a regular cast of the same.

The *dimensions* of the stones are a matter of great importance, for the severity of the symptoms that accompany any change of location of these concretions depends upon the relation which their size bears to the width of the gall-passages. These dimensions vary within very wide limits, generally standing in an inverse ratio to the number of calculi present—the more stones

[1] The Lancet, July 20, 1878.

[2] L. c., p. 299.

the smaller they are likely to be; the less, the larger. Exceptions to this rule, however, occur. From a practical point of view, it may not be without value to divide biliary calculi into three sizes, small, medium, and large, as follows: *Small* stones shall be considered as embracing those from the size of a grain of sand to that of a small pea. These are the most common, and occur in the largest numbers at once. *Medium-sized* stones are those from the size of a pea to that of a hazel-nut. *Large* stones, which are usually single, are of the size of a walnut and over up to the dimensions of a moderately filled gall-bladder. Very large stones are a rarity. Frerichs (l. c., p. 476) several times saw stones two to two and a half inches long and one inch thick. J. F. Meckel, in the "Transactions of the Berlin Academy," describes probably the largest gall-stone yet recorded. This was 15 ctm. long and 6 ctm. in diameter (6 inches by 2½). I recently had one given to me which was wedged into the gut, and measured 7.5 ctm. (3 inches) in length, 4 ctm. (1½ inch) in width and 12 ctm. (8¾ inches) in its largest diameter.[1]

The *shape* of gall-stones is extremely varied. In general the round or ovoid form predominates, though many polyhedral stones also appear. The latter often show facets, their edges and corners are usually rounded off, their flat surfaces appear ground, and are either plane or slightly concave or convex. The shape of a cube, of a three-sided pyramid, etc., are often encountered. In the bile-ducts of the liver we sometimes find cylindrical or even branching concretions studded with excrescences. Flattened, leaf-shaped stones, with a black surface and a metallic lustre, are rare, although Frerichs found nine specimens of them in a gall-bladder which contained none of a round or angular form. Tubular, coral-like concretions are very rare in man, but are said to be more frequent in cattle. In an individual who had died with all the symptoms of retention of bile, through occlusion of the ductus choledochus, Briquet[2] found tubular concretions, with a canal like that of a straw, following the ramifications of the bile-ducts to their finest branches.

[1] Compare *Leichtenstern's* work on Constrictions, etc., of the Intestines, this Cyclopædia, Vol. VII., p. 573, where other data will be found under this head.

[2] Dictionnaire encyclopédique des sciences méd., IX., p. 386.

Gall-gravel is a name given to concretions very minute in size and very large in number, of a black, brown, greenish, or white color. Gall-gravel occurs in connection with larger concretions, though also often found alone. Sometimes it is crystallized and granular, sometimes pulpy, consisting of mere inspissated bile. Cruveilhier once found the biliary passages from the ductus choledochus to the finest bile-ducts enormously distended and filled with such gravelly masses through which the bile flowed as through a sand-filter. Besnier saw a case in which the gall-bladder was filled with a soft, white, putty-like paste, which consisted almost entirely of cholesterine (perhaps crumbled cholesterine stones?). There are cases in which there is no sign of the formation of a concretion, and which really present only a bile-pulp. Thus Durand-Fardel found a greenish, semi-solid mass, of the consistency of glue, in the gall-bladder, which did not flow, which would remain clinging to the finger, and which did not escape from the gall-bladder, although the cystic duct was free.

The *color* of gall-stones shows every gradation from black, brown, yellow, to almost pure white. Most of them are brown, greenish or yellowish brown, the reddish and bluish shades being rare. The coloring-matter of the bile always constitutes the basis of the coloring. Most stones are opaque. It is only pure cholesterine stones that have a glassy transparency when they are fresh—when dry they are also opaque. Stones with a smooth cholesterine crust often have a pearly lustre.[1]

The *surface* of gall-stones is sometimes smooth, soft, and slightly greasy to the touch; sometimes it is uneven, rough and granular, so that it might be likened to a mulberry; in one case it may be covered with crystalline protuberances and clusters of crystals; in another it may present a worm-eaten appearance, covered with irregular furrows.

The *consistency* of most stones is but slight. They can generally be nicked with the finger-nail, and are easily broken and split. They are also easily ground down by their contact with one another. It is only the more rare lime-concretions, or those covered with a crust of the cholepyrrhin and lime compound, which present a stony hardness, at least in their crust.

With regard to the *specific gravity* of gall-stones—which is generally considered as being very light—we must not fail to

[1] In the ox, stones of highly irregular form are found which are quite hard and smooth, and which consist in the main of carbonate of lime with a shining, bronze-like coating of a pale yellow color.

distinguish as to whether they are fresh and moist, or dried. In their fresh state all gall-stones are heavier than water. Hein determined the specific gravity of a fresh cholesterine stone at 1027. In their dried state, when the water between the crystals has evaporated and been replaced by air, they generally float on the water. The only question of importance to be determined, however, is whether gall-stones float in the bile. As the specific gravity of the bile is 1020 to 1026, reaching in extreme cases 1046, it is evident that cholesterine stones, of a specific gravity of 1027, may, under some circumstances, float in the bile. But most gall-stones exceed 1027 in specific gravity. Those which, in addition to pigment matter and bile-resin, also contain salts of lime, are even much heavier, mounting, according to Bley, to 1580, and according to Batillat,[1] to 1966.

The *structure* of gall-stones arouses our special interest, because it leads us to conclusions with regard to the conditions of their origin, and the processes of their growth. The older physicians already occupied themselves with the structural conditions of gall-stones, this study being carried on with special diligence by F. A. Walter (1796), with the assistance of the material afforded him by the anatomical museum of Berlin. In later times Stein, H. Meckel, Fauconneau-Dufresne, and Frerichs have especially occupied themselves with this matter.

Walter distinguishes three kinds of gall-stones, according to their structure, viz., the striated, the lamellated, and those provided with a shell or rind. The striated ones, on section, show lines radiating from the centre toward the periphery. The lamellated variety show layers concentrically arranged around a centre, like an onion. Those provided with a rind (the "capilli corticati"), to which class the majority of gall-stones belong, show a nucleus, a middle zone of very variable composition, and an external rind. We would retain the following division of gall-stones as appropriate and practical. It was developed in its outlines by Fauconneau-Dufresne, and elaborated by Frerichs. It divides stones into the simple or homogeneous, and the compound.

1. *Simple homogeneous stones*, of entirely uniform structure, occur comparatively seldom. Their fracture is earthy, soap-like, or crystalline. The stones with a crystalline fracture (often of

[1] Compare *Frerichs*, l. c., p. 478.

the striated variety) consist of pure crystallized cholesterine; those with an earthy or soapy fracture consist of the earths or of an intimate mixture of biliary fats and the cholepyrrhin and lime compound; they may also consist of bile-resin, or its compound with lime, or of cholesterine and soaps.

2. *Compound nucleated stones* generally present three parts, viz., a nucleus, a shell surrounding this, of variable thickness, and finally, a crust or rind. The latter part, viz., the rind, is sometimes absent.

a. The *nucleus*, commonly of a brown or black color, generally consists of the cholepyrrhin and lime compound, bound together by the mucus that is intermingled with it; more rarely it also contains carbonate of lime, or is formed by a cluster of cholesterine crystals. In fresh stones the nucleus is full (solid or semi-solid), in dried ones it is often fissured. There are positively no definite relations between the size of the nucleus and the thickness of the middle zone, or of the external crust. The nucleus is generally situated in the centre, though sometimes it is eccentric. Some biliary concretions have more than one nucleus. Bouisson found two; Fauconneau-Dufresne observed four nuclei in a stone of pyramidal form; Guilbert claims to have seen five. Stones thus composed evidently consist of originally separate smaller stones, which have been agglutinated by the mucus in the bladder and have thus served as nuclei for the common external layers.

In rare exceptional cases the nucleus of a gall-stone consists of a foreign body. Bouisson observed a little black lump in a small, solitary, and probably recent stone, which, on microscopic examination, proved to consist of red blood-corpuscles. The best known case is that of Lobstein, who found a stone in the ductus choledochus of a woman, sixty-eight years old, the nucleus of which was formed by a round-worm. Bouisson found a very soft stone of the size of an almond in the bile-duct of an ox, the nucleus of which showed a fragment of a distoma. Nauche[1] found an incrustation of the size of a small nut in a shrivelled and wasted gall-bladder, which had formed around a needle 2 ctm. long. The oxidized needle lay in a sack-shaped pouch formed by the wall of the bladder, the point of the needle being outside of the latter. Lacarterie[2] tells of a stone as

[1] Lancette francaise, 1835, 17th Sept.

[2] Gaz. de santé, 1827, 25 Avril. Cited by *Fauconneau*, l. c., p. 104.

large as a plum, consisting chiefly of cholesterine, the nucleus of which, melted by warmth, showed numerous globules of quicksilver. The individual in question had been given the gray ointment, by inunction, for syphilis. Beigel[1] likewise detected little globules of quicksilver, by means of a magnifying glass, in a brown gall-stone. In a gall-stone, belonging to the Göttingen collection, which weighed four ounces, Fuchs and Frerichs[2] found a plum-stone as a nucleus. The stone lay in an abscess of the liver which had arisen as a result of a perforating gastric ulcer.

b. The *middle zone* (the *shell*), interposed between the nucleus and the external crust, presents a very variable appearance. It is not, however, always present; sometimes the crust immediately covers the nucleus. This middle zone is most frequently striped in a radiate form, composed of little plates of cholesterine disposed in a radiate manner, and therefore having a glistening, crystalline appearance. It also often presents an arrangement in concentric layers. Biliary coloring matter is often mingled with the cholesterine, whereby its crystalline appearance is destroyed. This layer is generally of a brownish or yellowish color, often softer than the crust, especially when it is rich in coloring matter. In some cases the shell is devoid of structure; it is of a soapy or earthy consistency, showing neither stripes nor layers.

c. The *crust* or rind can be distinctly distinguished from the middle zone by its color, hardness, and laminated structure. Its thickness varies much in different specimens, but is generally uniform. Sometimes the surface of the crust is studded with warty projections. It is only exceptionally that this crust is found wanting, the radiating cholesterine plates of the middle zone then extending to the surface, and here terminating in warty elevations or in combs. The composition of the crust varies. It consists either:

1. Of *cholesterine*, generally in the shape of smooth layers, sometimes separated from one another by pigment, which cover the round or polyhedral stones, giving them a pearly, lustrous, smooth coating, almost white, or from a pale yellow to a greenish gray color. Sometimes this cholesterine crust forms crystalline projections. Or,

[1] Wiener med. Wochenschr. 1856. No. 15.

[2] L. c. II., p. 480.

2. Of the *cholepyrrhin and lime compound,* an extremely hard, very thin, smooth covering (about 1 mm. thick) of a greenish black hue. Or,

3. Of *carbonate of lime.* This lime-crust sometimes constitutes a thick brown envelope of an earthy fracture; sometimes a white, smooth covering, consisting of several layers separated by pigment deposits; or, again, a warty coating, or one armed with thorns when the lime is deposited in rod-shaped crystals.

Chemical Composition of Biliary Concretions.

The substances that are found in biliary concretions are all of them also to be found in the bile, or arise from the decomposition of substances found there. The most important of these are as follows:

1. *Cholesterine.*—This forms the chief constituent of most gall-stones, some of them being formed entirely of this substance, and but few being altogether devoid of it. Cholesterine generally occurs in a crystalline form, though it is also found as an amorphous substance, intimately combined with coloring matters, soaps, etc. It is estimated that the majority of gall-stones contain an average of from 70 to 80 per cent. of cholesterine, whereas the bile is notoriously poor in this ingredient. (According to Frerichs, normal human bile contains $\frac{26}{100}$ per cent. of gall-stones; according to Robin, from $\frac{16}{100}$ to $\frac{26}{100}$ per cent.) Cholesterine is held in solution in the bile by the alkaline salts of the biliary acids; its slight solubility favors its separation in solid form.

2. *Biliary coloring matters* are to be found in variable quantities in nearly all gall-stones; their absence may be regarded as the rare exception. The most important of these coloring matters is cholepyrrhin, which occurs in part pure and in part chemically combined with lime. Cholepyrrhin generally constitutes a material ingredient of the nucleus, often also of the middle zone, but is especially to be found (as a compound of cholepyrrhin and lime) in the crust. It is insoluble in water and alcohol, slightly soluble in ether, and readily so in chloroform. The biliary coloring matters are readily soluble in alkaline fluids.

The alkaline salts of the biliary acids dissolve cholepyrrhin in moderate quantities. Coloring matters occur in normal human bile in the proportion of $\frac{14}{10}$ to $\frac{30}{100}$ per cent.

3. *Biliary acids and their salts.*—In most gall-stones small quantities of biliary acids are found combined with an alkali (soda). They can be extracted by water, but more completely by alcohol. Combinations of the biliary acids with lime, which are sparingly soluble in water, but more readily so in alcohol, have been found in human gall-stones.

4. *Fatty acids* (stearic acid) are seldom found in any considerable quantity in human gall-stones. On the other hand, combinations of these acids with lime are very commonly to be found there. According to Frerichs, some stones consist mainly of margarate of lime. One specimen examined by him contained 68 per cent. of margarate of lime, 28 per cent. of cholesterine, and 3 per cent. of cholepyrrhin and lime-compound and mucus.

Some authors mention *uric acid* as an ingredient of certain stones. Aside from those gall-stones which have passed into the urinary bladder through fistulous openings, and remained there (see below), a mistake might here be made from the fact that the supposed biliary calculi, which contained uric acid, are actually urinary calculi, which had accidentally become mingled with the biliary calculi in the museums.

Lime is the only one of the inorganic substances which, by reason of its quantity, constitutes an important ingredient of gall-stones. Iron, which was always found by Frerichs, manganese, more rarely found, and copper, never missed by him in any large human stone containing coloring matter,[1] as well as the quicksilver occasionally demonstrated, after all only appear in minimum quantities, and none of them, unless we may except the quicksilver, are of any significance in the development of the concretions. But it is different with lime. Aside from the lime found in combination with cholepyrrhin or with the fatty or biliary acids, *carbonate of lime* is particularly to be mentioned as an ingredient of many gall-stones. Compared with this, the phosphate and sulphate of lime, as well as the corresponding

[1] *Bertozzi* and *Heller* (1845) demonstrated this in pitch-black pigment-concretions.

magnesia salts, appear in but insignificant quantities. Some concretions from the biliary passages consist exclusively of earthy substances and principally of carbonate of lime. Generally, however, the lime-salts only form an incrustation of the actual gall-stone. They originate, in great part, from the mucus of the gall-bladder, which contains this ingredient, and they are especially liable to be precipitated when the gall-bladder contains no more bile.

Such a stone, found by Bailly in a bladder containing only mucus, and analyzed by O. Henry, consisted of 72.70 per cent. of carbonate of lime, 13.51 per cent. of phosphate of lime, 2.98 per cent. of oxide of iron, and 10.81 per cent. of coloring matter, mucus, etc. Andral also analyzed a white stone which he found in a gall-bladder containing only mucus (with an obliterated cystic duct). This stone is said to have consisted exclusively of posphate of lime.

Gall-stones may be classified as follows, according to their chemical composition—that is, according to the predominance of one or another of their components:

A. Concretions containing Cholesterine. These are divided again into

1. *Pure, simple, cholesterine stones.*

These are generally single, or there are but few together, and, on the whole, they are not very frequent. They are roundish, of the size of a pea to a large cherry, of glassy transparency, colorless, or of a faint grass-green, their surface is smooth, granulated or nodular, their fracture shows radiate crystalline plates, and is, therefore, glistening. They are of light specific gravity, not hard, easily cut.

2. *Mixed cholesterine and pigment stones* (with a slight admixture of salts, etc.).

This is the commonest form, several or even many being found together, of all sizes and shapes. They are often faceted, are externally of a brown or green color, or are covered with a pearly, shining, smooth coating of cholesterine. Their fracture shows concentric layers of changing color and different degrees of lustre. They often possess a crust (see above) of lime and pigment (hard, dark green, smooth), or of carbonate of lime (white), which sometimes forms a

uniform, smooth cover, sometimes appears in coarser crystalline clusters, rough and jagged masses. Aside from this lime-crust, these stones are of light specific gravity and quite soft.

B. CONCRETIONS DESTITUTE OF CHOLESTERINE. Of these there are two varieties, viz.:

1. *Pure, simple pigment-stones.*

These are not especially frequent. They are very small, often gravelly, generally occurring in large numbers. The larger ones are mulberry-shaped, blackish green, shining like tar, their fracture is likewise so, and they are homogeneous. They are not very firm, and their specific gravity is light. They are notable for the amount of copper they contain.[1]

2. *Simple lime-stones* (carbonate of lime).

These are very rare, are single, of heavy specific gravity, very hard, and of a whitish gray color. Their surface is rough, or even slightly warty.

The following table, which is taken from Gorup-Besanez' Handbook of Physiological Chemistry (3d edition, 1874, p. 536), may serve to illustrate the quantitative composition of gall-stones. From the figures given it is evident that the analyses refer to stones of the most varied composition:

In 100 parts by weight of the stone there were as follows:	1. Chevalier.	2. Von Planta and Kekulé.	3. From Gmelin's Handbook.	4. Ditto.	5. Joyeux.	6. Marat.	7. Brandes.	8. Phipson.
Cholesterine	96.	90.82	65.	50.	4.	—	69.76	1.35
Biliary coloring matter	3.	0.20				—	11.38	61.36
Saponifiable fat	—	2.20	25.			—	—	—
Mucus	—	1.35		35.	89.	—	13.20	11.50
Biliary matter	—	0.79	3.			—	5.66	2.75
Salts	—	0.28	2.	8.	3.	100.	—	13.65
Water	—	4.89	—	—	—	—	—	8.00

[1] Not long ago I had some such pigment-stones analyzed by Professor Hüfner and they were found free from copper.

Ritter (Robin's Journ. de l'anat., etc., 8 me année, 1872, p. 60) distinguishes eight classes of gall-stones according to their structure and their general external conditions, and gives the following analysis of these varieties. The last line shows the number of specimens included in each category.

	1.	2.	3.	4.	5.	6.	7.	8.
Cholesterine	98.1	97.4	70.6	64.2	81.4	84.3	A trace.	0.
Organic matter	1.5	2.1	22.9	27.4	15.4	12.4	75.2	18.1
Inorganic matter	0.4	0.5	6.5	8.4	3.2	3.3	24.8	91.9
Number of specimens	28	16	580	94	220	16	3	1

For some interesting details of Ritter's analyses compare the original cited above.

Mode of Origin of Gall-Stones.

The mode of origin of gall-stones has always been a subject of much thought with physicians, evidence of which may be found in the manifold attempts to explain the phenomenon, both in older and more recent times. The unfamiliarity of the older physicians with the chemistry of the bile and its concretions caused them to account for the development of the latter on mechanical principles. Even Boerhave and van Swieten thought there was no doubt that gall-stones were produced by the bile stagnating in its passages, thickening, drying, hardening, and finally falling into fragments which presented themselves to us as gall-stones. Inspection of the fracture of an ordinary laminated cholesterine and pigment-stone ought to have shown the fallacy of this explanation. In more recent times chemical processes have been brought forward as explaining the development of gall-stones, without our undervaluing, at the same time, the influence of mechanical causes. The differences in the structure and chemical composition of gall-stones would lead us to expect that various chemical processes were concerned in their production.

The process that takes place in the development of gall-stones

consists in this: that those components of the stones which exist in a soluble state in normal bile separate themselves in solid form, are thrown down, and unite into a conglomerate mass. We shall naturally first consider those substances found in the nucleus of the stone, and which therefore constitute its first deposit, viz., cholepyrrhin, pigment-lime, cholesterine, and cholate of lime. Simple concentration of the bile cannot effect the separation of those substances; in fact they remain in solution as long as the bile has undergone no change.

The process of precipitation of previously dissolved constituents of the bile therefore implies that some deviation from the normal chemical constitution of this fluid, either quantitative or qualitative, has taken place. And it further presupposes a retardation or temporary interruption of the flow of bile, for a certain degree of rest and stasis of the fluid is necessary, or, at least, highly desirable for the agglomeration of the precipitate. Add to this the fact that in stagnating bile the influence of the mucus of the gall-bladder readily causes decomposition of the biliary salts of soda, whereby occasion is likewise given for the development of stones. We may therefore regard the decomposition and stasis of the bile as the universal antecedent, that is, as the cause of the formation of gall-stones.

With regard to the first circumstance, viz., the alteration of the biliary fluid, the following points are to be considered:

1. Certain substances may arise in such quantities in the bile that the solvents always provided for them are not sufficient to hold them entirely in solution. This has reference especially to cholesterine. Its slight solubility in the bile, that is, in a solution of tauro-cholate of soda, must occasion a precipitation of this substance as soon as it is present in excess in the bile (therefore in the liver and in the blood). Frerichs considers it probable that the frequent occurrence of gall-stones in old people is connected with the increased amount of cholesterine in the blood of such persons; in which case it would still remain to be proved that the increase of cholesterine in the blood was associated with a corresponding increase in the bile. Such a correspondence must be regarded as highly probable.

2. The bile, which under normal conditions has an alkaline

reaction, sometimes, under certain influences, becomes more or less *acid* in the gall-bladder. In protracted ill-health, when the bile remains stagnant for a longer time in the bladder and becomes thickened, we may suppose that this acid condition arises under the influence of the mucus of the gall-bladder. We know from experiments on animals that the acid reaction of the bile increases under an exclusively meat diet, while it never develops spontaneously under an exclusively vegetable diet. Under the influence of an acid condition of the bile, the decomposition of cholate of soda and analogous matters, which ordinarily hold the cholesterine and biliary matter in solution, is accomplished, so that these substances are precipitated. Under such circumstances any clot of mucus or of blood may become the centre around which these precipitated substances are deposited, and thus a stone is formed.

3. The natural solvents for certain substances may be present in insufficient quantity, or new and surplus elements may arise in the bile which are capable of separating the cholesterine and the biliary coloring matters. Thus Thénard attributes the separation of the biliary coloring matter to a diminution of the soda salts in the bile. The other process is referred to by Bramson, when he attributes the separation of biliary coloring matter under the form of the cholepyrrhin and lime compound to an excess of lime in the bile. Verheyen (1856) arrived at a similar conclusion with regard to gall-stones in animals, when he said that every excess of lime in the bile enters into an insoluble combination with the coloring matter of the same, the lime partly taking the place of the soda, and thus diminishing the solvent power of the cholate of soda. An argument in favor of this is found in the fact that the nucleus of most gall-stones consists of cholepyrrhin.

So far as the lime is concerned with which the cholepyrrhin, the fatty acids, and the cholic acid in the gall-stones are largely combined, the amount found in normal bile is known to be very small, nor do we know that, under any circumstances, an excess of lime does arise in the bile. For this reason Frerichs does not think that the lime of biliary concretions is furnished by the liver—that is, by the bile—but regards it as supplied,

in greater part, by the mucous membrane of the gall-bladder. In support of this view he states that he has repeatedly found the mucous membrane of the gall-bladder covered with numberless crystals of carbonate of lime, and also refers to the finding of a gall-stone which lay in close contact with the wall of the bladder, its free surface, which was bathed in bile, being studded with cholesterine crystals, while that portion of the stone which touched the walls of the bladder was covered with a thick crust of carbonate of lime. Experiences of this kind, as well as other circumstances, testify to the significance of catarrh of the gall-bladder in the development of calculi.

In the further *growth* of gall-stones the same chemical alterations probably come into play which have here been discussed in connection with their beginnings or nuclei. But the structure of the stones and their so frequent laminated character would lead us to suppose that the chemical conditions and pathological alterations of the bile, in any given case, undergo a certain periodical change. It is true that the circumstances on which the manifold and varying structure of the concretions, in individual instances, depends are unknown to us. Nor do we know anything more positive with regard to any possible *secondary* metamorphoses which the gall-stones might undergo after their development in the organism, as H. Meckel has tried to make us think probable.

In connection with the question of the origin and growth of gall-stones we encounter the further question concerning certain *destructive processes* to which these concretions are sometimes exposed during their sojourn in the organism. As this includes the matter of the solution, the crumbling, the diminution in size of the concretions, a certain significance is attached to the subject from a practical, therapeutic point of view.

It is undetermined whether gall-stones which have once been developed can undergo complete chemical solution, and thus disappear. We cannot deny outright the possibility of such an occurrence, in view of the fact that the partial solution or arrosion of concretions, that is presently to be mentioned, is established beyond a doubt. The solution of gall-stones in the human body, under the influence of certain medicines (Durande's rem-

edy, the internal use of chloroform, etc.), has been claimed by various parties as a positive fact.

Attrition of the stones on one another does not take place as often as their form has led authors to believe.[1] And yet O. Wyss (Betz' Memorabilien, XVII. 1872, p. 1) ascribes to this grinding process a prominent rôle among the factors which may cause the crumbling of gall-stones.[2] The flat surfaces caused by the mutual attrition of stones have generally a different color from the other surfaces of the stone, and show distinct concentric stripes if the grinding process has attacked cholesterine layers of different colors. The extent to which a stone may be encroached upon is very variable; sometimes a single ground surface extends almost to the nucleus, indeed the nucleus itself, and therefore the larger part of the entire stone may thus be made to disappear. A stone may, of course, be still more diminished in size if it is exposed, at the same time, to two or three grinding surfaces. In addition to being thus ground down, a concretion is sometimes the seat of radiate fissures, whereby its destruction is hastened. Wyss even explains the favorable action of certain mineral-waters (alkaline, etc.) in cholelithiasis, on the hypothesis that active peristaltic movements of the gall-bladder are called forth by these waters, thus inducing the prolonged rubbing together of the gall-stones and their mechanical diminution in size, and facilitating their passage into the intestine, and expulsion.

Erosion and crumbling of the stones are not rare processes, and on this ground alone deserve our attention.

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[1] The stones with facets, which are so frequent, do not, as a rule, arise from this grinding process. On making a transverse section of these, one is convinced that the superficial layers are deposited parallel with the flat surfaces, that they are, therefore, not cut through by the facets, whereas the central layers gradually assume the globular form. This would prove that the facets originate with the growth of the stone itself, and in so far represent its primary condition. The faceted stones owe their shape to the peculiar spatial relations within the bladder at the time of their origin. Their development seems to proceed in this way, that the spaces remaining between the calculi, which at first touch one another lightly, are gradually filled up with new laminated deposits.

[2] As such factors, H. Meckel (Mikrogeologie), Frerichs, and others adduce the occurrence of radiate fissures in stones, carious erosion, and the erosion in the form of flattened losses of substance caused by the bile.

So far as erosions are concerned, we sometimes encounter gall-stones which present cavities and defects similar to those of carious teeth. These erosions are sometimes superficial, perhaps destroy only the cholesterine coating of the stone at a circumscribed spot, or they pass through several layers, even to the nucleus itself. We will leave undecided the question of how far chemical processes come into play in the production of these changes. It is generally taken for granted that the fluids surrounding the stone exercise a solvent influence on the layers. If the bile were rich in the alkaline salts of the biliary acids it might, it is true, dissolve at least the cholesterine and perhaps also the compound of cholepyrrhine and lime.[1] But it seems to us a circumstance worthy of note, because opposed to the theory of a process of simple chemical solution, that the erosions in question do not attack entire layers of a given chemical constitution but that they destroy different layers in a similar manner, though locally circumscribed. I, therefore, conclude that causes are here at work which operate locally, and as this does not apply to the bile, which, as a fluid, must come equally in contact with the entire surface of the concretions, I should not know what other agency to think of but that of certain of the lower organisms (bacteria). These, indeed, fulfil all the conditions here existing. Bacteria are often present in the bile, especially if abnormal secretions and similar pathological processes are in progress in the mucous membrane of the gall-bladder. Bacteria live principally on the mucus and other organic materials which are enclosed within the concretions, and by consuming these, within a certain area, they render the cholesterine layers porous and prepare them for mechanical crumbling. Indeed, the analogy between caries of teeth and caries of gall-stones is not to be ignored.

[1] I recently came across an admirable example of this kind. The gall-bladder, which was filled with a number of chiefly small, laminated, cholesterine-pigment stones, and was contracted closely upon its contents, showed a perforation that was occupied by a concretion of the size of a cherry. Besides the calculi, the bladder contained only a little bile largely mixed with mucus and pus. A number of stones, hardly as large as a pea, were more or less extensively eroded in the manner described. In some of them the cholesterine layer lying between the nucleus and the external crust was almost entirely dissolved, and of the crust itself but a few small arches remained, wide enough to prevent the dropping out of the nucleus.

The *splitting* and *crumbling* of gall-stones into a number of larger or smaller fragments has likewise been observed quite frequently. Such fragments are occasionally met with in the gall-bladder and its ducts on the dead body, or in the stools of persons suffering from gall-stones, and, according to the circumstances of the case, may sometimes be fitted to the original concretion from which they were broken. Only those stones which are possessed of an inferior degree of firmness seem to be liable to this mechanical injury, particularly the common cholesterine-pigment calculi. The pressure of the strongly contracting gall-bladder, as well as the resistance which the concretions meet with from the walls of the ductus cysticus and choledochus is sufficient to break them, especially if, at the same time, several stones are pressed against one another. Even during their progress through the intestines stones might possibly undergo the process of crumbling.

Etiology.

The immediate cause of the formation of gall-stones is to be found in certain chemical alterations in the bile, occurring coincidently with the prolonged stasis of this fluid, or at least with a retardation of its flow. Numerous conditions of the most varied kind are regarded as favorable to the development of gall-stones, and are consequently adduced, with greater or less justice, as remote or predisposing causes of this affection. These conditions will be discussed below.

1. *Age* plays an important part among the predisposing causes of cholelithiasis. Although gall-stones have been found in persons of every age, even in new-born children (see below), still this much is certain, that they are very rare before the age of twenty-five, tolerably frequent after the age of forty, and attain by far their greatest relative frequency in old age. In 395 cases collected by Hein, he found only fifteen persons under twenty-five years old, and only three of these were under twenty (viz., a girl of eighteen, another of seventeen, and a boy of sixteen). Similar results are obtained from the figures collected by Walter, Fauconneau-Dufresne, and others; but the entire num-

ber is still too small to determine accurately the relative frequency during the different periods of life. The material on hand is not even sufficient to determine the question of whether the maximum of frequency in the female sex falls within the same period of life as in the male sex, and whether there may not be two maxima—at least for the female sex, as it appears—the one of which would fall at about the fortieth year, and the other in old age. Indications of this sort would seem to be given by the following figures of Durand-Fardel from 230 cases, all of which were diagnosticated by himself as biliary colic, due to gall-stones:

	Women.	Men.	Total.
Under 20 years	1	1	2
From 20 to 30 years	25	3	28
" 30 " 40 "	40	13	53
" 40 " 50 "	28	30	58
" 50 " 60 "	32	19	51
" 60 " 70 "	12	18	30
" 70 " 80 "	4	4	8
Total	142	88	230

Durand-Fardel regards the great number of instances occurring between the age of thirty and forty in women as standing in a causal connection with pregnancy, which is thought to favor the development of gall-stones.

So far as biliary concretions in children are concerned, these generally present themselves in the shape of little white concretions of coloring matter within the inspissated bile of the bladder. Portal and Bouisson have seen new-born children who were highly jaundiced, and whose autopsies revealed a large number of concretions of the size of a pea, partly in the gall-bladder and partly in the biliary passages, especially at the point of entrance of the ductus choledochus into the duodenum.[1]

[1] Fauconneau-Dufresne, l. c., p. 136.

The rare occurrence of gall-stones during childhood and youth has been thought to have some connection with the greater activity of the biliary secretion, as well as with the increased sensitiveness of the receptacles of bile, which are stimulated to energetic and continuous efforts at emptying themselves on the first beginning of any stone-formation. With increasing age the gall-passages grow, to a certain extent, more tolerant of solid bodies within them, prolonged stasis of bile takes place more easily, and the concretions are allowed a longer period of rest for growth. With age an increase of precipitable substances appears in the bile, particularly of cholesterine, which is developed more abundantly in proportion to the increased retrograde metamorphosis taking place in the body. Perhaps something similar is true of lime as of cholesterine.

2. *Sex.*—The formation of gall-stones takes place decidedly oftener in the female sex than in the male. This unmistakable fact was pretty generally known to physicians as early as the middle of the last century. Among 230 cases collected by Durand-Fardel (1868), within his own field of observation, 142, or 62 per cent., were in females, and 88, or 38 per cent., in males. This proportion agrees pretty well with the figures of Hein, according to which, in 620 cases, 377, or 61 per cent., occurred in females, and 243, or 39 per cent., in males. The liability to the disease in the two sexes would therefore be about in the proportion of 2 : 3. The causes of the preponderance of the disease in the female sex are anything but plain. It is natural first to seek for these in the sexual functions of the woman. But even the fact, as such, that the formation of gall-stones in the female sex is influenced or favored by the sexual functions is not established ; much less can we demonstrate any intimate relation between this abnormal condition and the processes of menstruation, pregnancy, etc. According to Soemmering, biliary calculi are noticeably more frequent in those years when menstruation ceases. Willemin, on the contrary, states that the beginning of cholelithiasis in women does, indeed, sometimes occur at the change of life, but that he has also seen instances in which previously existing attacks of this affection have ceased with the close of the menstrual epoch. Among the external conditions by which it has been sought to

explain the more frequent occurrence of gall-stones in the female sex, we may mention the peculiarly sedentary habits of life of women, as well as the unwise use of corsets, which constrict the region of the liver.

According to Fiedler, 4,300 autopsies were conducted in the Dresden City Hospital in the seventeen years from 1853 to 1869 inclusive, and among this number the presence of gall-stones is mentioned in the notes in 270 cases (7 per cent.). But Fiedler remarks that in reality this number is too low, as the condition of the gall-bladder is often not mentioned. Fiedler's notes with regard to the occurrence of gall-stones in the several different years are worthy of notice. These concretions were found during the years 1853 to 1869 in the following percentage of the autopsies conducted each year, viz.: 9.5, 14.0, 9.2, 7.9, 9.8, 6.7, 4.2, 4.2, 6.1, 5.0, 5.2, 4.5, 6.4, 4.7, 6.4, 5.2, and 4.1 per cent. The larger percentage occurring during the early part of this period is due in part to the fact that at that time a larger proportion of older people was admitted. At the same time, there is no denying the possibility that other unknown circumstances may have had an influence on these numbers. Among 2,511 male bodies, gall-stones were found ninety-eight times (3.9 per cent.), while among 1,789 female bodies they were found 172 times (9.6 per cent.). During the years 1853 to 1869 the following per cent. of *all female* bodies examined were found to contain gall-stones, viz.: 17.1 15.0, 12.2, 16.4, 9.4, 9.3, 6.2, 6.6, 8.5, 6.7, 9.1, 6.7, 12.9, 7.0, and 7.3 per cent. Of the 270 bodies containing gall-stones, 36.3 per cent. would therefore belong to the male sex, and 63.7 per cent. to the female sex, a proportion which corresponds very nearly with that obtained from other sources (see above). Only three of those 270 persons affected with gall-stones were under twenty years of age (seventeen to nineteen years old).

3. *Conditions of the Soil, Climate, Season of the Year, Social Condition*, etc.—With regard to any influence which the agencies mentioned above may have on the frequency of the formation of gall-stones, we can find only imperfect and occasional statements to which no great value can be attached, because they are based on mere estimates, and not on positive figures. Cholelithiasis is said to be strikingly frequent in Hanover (Haller, Soemmering, Canstatt), in Lithau (J. Franck), in Suabia, England, Hungary (Canstatt). In Vienna, according to J. Franck, at least every tenth body is found to contain gall-stones. According to my own experience, the comparative frequency of the disease in Suabia would not seem to be great, but I also can furnish no positive figures. On the other hand, it is claimed that gall-

stones are very rare in Holland (Brugmans), and probably also in Finland; at least, a very experienced physician from Helsingfors recently told me that in all the numerous autopsies he had attended at home he had never seen a gall-stone. The attempt has been made to explain the frequency of gall-stones in a certain given region by the character of the drinking-water, especially by the fact of its containing a larger amount of lime. But these theories are by no means sustained by sufficient evidence.

The same uncertainty exists with regard to *climate*.[1] It has been assumed that the abundant secretion of bile in hot climates antagonized the development of gall-stones (J. Franck), and thence concluded that gall-stones must be rare in hot climates. But this is by no means proved. Saint Vel,[2] for instance, believes that cholelithiasis is as frequent in excessively hot as in temperate climates, and equally so in the negro as in the white man.

The *seasons of the year* seem to exert no noticeable influence on the frequency of this disease in man.

So far as *social conditions* are concerned, gall-stones are more frequent among the favored classes than among working people, and among the latter the agricultural class is said to be more exempt. It is certain that biliary colic is less frequently met with in hospitals than in private practice. Amongst the large number of patients treated in all the hospitals of Paris there were but seventy cases of biliary colic to be counted in 1861, and ninety in 1862.[3] The cause of all this is no doubt principally to be found in the influence exerted on the development of gall-stones by sedentary methods of life (see below) and different kinds of nourishment.

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[1] Compare *Hirsch*, Hdb. d. hist. geogr. Pathol., II., p. 32: "Gall-stones likewise appear (in a striking manner) to be more rare in the tropics than in the temperate zones. Annesly and Twining, it is true, mention them among the diseases of India, but Morehead, on the other hand, remarks that while practising there for many years he only saw four cases; and Pruner also declares that the affection is more common in Europeans and Turks than in native-born Egyptians and negroes. In European Turkey, Rigler says, gall-stones are frequent."

[2] Traité des maladies des régions intertropicales, Paris, 1868.

[3] Dictionn. encyc. des sciences méd., IX., p. 400.

4. *Heredity.*—According to Fauconneau-Dufresne, cholelithiasis is often hereditary. He bases this assertion on the experience of the bath physicians (at Vichy) who so often have the opportunity of observing liver diseases of all sorts. This point requires still further elucidation.

5. Certain *diatheses* and *faults of constitution* have repeatedly been adduced as causes of the development of gall-stones, or at least, as circumstances favorable thereto, but do not seem to me to play any special rôle in this direction. When one man calls attention to the frequent occurrence of gall-stones in the victims of cancer, or another (like Durand-Fardel) to the coexistence of cholelithiasis with chronic cutaneous eruptions, psoriasis, eczema, and the like, it is not at all necessary to fall back on a diathesis to explain these facts. Such cases, in fact, do not seem to present anything more than an accidental coincidence of two diseases which are both of them quite frequent at certain periods of life. Among the older physicians the *gouty* diathesis was especially cited among the causes of cholelithiasis, and, as it would appear, unjustly so. The simultaneous occurrence of gout and biliary calculi in an individual is not very frequent. If the physicians at watering-places (for instance, at Karlsbad or Vichy) often observe the coincidence of these two diseases, the peculiar circumstances under which they practice forbid our accepting it as evidence of what would hold good on a general average. It is only necessary to remark how seldom women suffer from gout, while they afford a much larger proportion of the cases of gall-stones than the male sex, which is especially liable to gout. And why should not gouty patients sometimes suffer with gall-stones, since various circumstances which favor the development of gout also notoriously contribute toward the formation of gall-stones, as, for instance, more advanced age, sedentary habits of life, the prolonged bodily rest compelled by the paroxysms of pain, habitual dyspepsia, etc. At all events, no proof has yet been brought forward of any intimate causal connection between gout and the formation of gall-stones.

As Frerichs has already declared, there is absolutely no ground for recognizing a peculiar diathesis for the production of gall-stones, an analogue to the uric acid diathesis, which, like

the latter, might be based on anomalies of tissue metamorphosis. For gall-stones occur in the most different constitutions, while their dependence on general disturbances of tissue metamorphosis cannot be demonstrated.

Corpulence is also frequently assigned as a cause of the development of gall-stones. Cholelithiasis certainly does occur often enough in corpulent people, although it is well-known that very lean people are also affected in the same way. But the one is not caused by the other. A similar relation seems to exist between these two affections as between gout and the formation of gall-stones, inasmuch as the circumstances which contribute toward corpulence also favor the development of gall-stones.

Quite recently Beneke[1] has called attention to the frequent coincidence of gall-stones with atheromatous degeneration of the arteries and excessive fat-development in the body. His conclusions are based on the examination of 375 dead bodies, 30 of which (8 per cent.) had gall-stones, while atheromatous degeneration was found in 114 (30.4 per cent.). Of these 30 cases of gall-stones, 22 (73.3 per cent.) were coincident with atheroma of the arteries (in 13 of the 22 the atheromatous process was very far advanced), and in only 8 cases (26.6 per cent.) of gall-stone was there no degeneration of the arteries. According to Beneke's showing it would appear as if the occurrence of gall-stones at an earlier period of life (from twenty to thirty years of age) was connected with a somewhat earlier development of atheromatous degeneration of the arteries, for among 22 cases of gall-stones with atheroma, 4 (almost 22 per cent.) occurred between the age of twenty and thirty, while among 92 cases of arterial degeneration without the simultaneous existence of gall-stones only 9 cases (10 per cent.) happened at the same time of life. According to Beneke's observations both the development of gall-stones and atheromatous degeneration of arteries are frequently accompanied by the abundant and even excessive development of fat within the body. Beneke, however, reserves his judgment as to the causal relation between the processes of gall-stone formation, atheromatous degeneration, and fat-development. It is

[1] Deutsch. Arch. f. klin. Med. XVIII. 1 Heft. 1876.

worthy of remark, however, that he is not inclined to regard the more abundant production of cholesterine as a cause of the formation of gall-stones.

6. A *faulty diet*, particularly one too largely composed of meat, indulgence in very fat food and in spirituous drinks, are among the causes which one often hears assigned for the development of gall-stones. It is hard to say how much truth there is in this statement. For gall-stones are often enough developed under diametrically opposite conditions of diet, and many people remain exempt in spite of indulgence. It will not be denied that diet has an influence on the formation of gall-stones, but this influence cannot, as yet, be scientifically defined, and all evidence is wanting for any direct connection between the two. For it is probably not by their mere introduction that an excessive meat diet or fat diet are injurious, but from the fact that they disturb the digestion and the secretion of bile in a general way. In the employment of alkalies for cholelithiasis we aim not so much at a direct chemical alteration of the bile as we do at the restoration of normal digestion and the secretion of bile generally.

Among the pathogenetic influences lying at the foundation of the development of gall-stones, those circumstances occupy an especially important position which cause a retardation or arrest of the flow of bile, because it is easier to see their method of operation. Among this class we may reckon the following:

7. *Too long an Interval between Meals.*—During these intervals the bile retained in the gall-bladder is in a state of comparative rest. Any precipitates that may be present have time to form themselves into concretions. Frerichs, who has called attention to this fact, thinks that the delay of the bile in the gall-bladder is of more significance, as regards the formation of stones, than the character of the nourishment or the general condition of nutrition.

8. *Sedentary Habits.*—Everything that puts an individual at rest, bodily, and keeps him so, interferes with the flow of bile, and thus favors the development of concretions. This applies, then, not only to so-called sedentary habits, which render cholelithiasis so comparatively frequent a disease among women, among scholarly men, and among the better classes of society;

it also holds good with regard to prolonged confinement to bed in tedious diseases (S. Cooper, Willemin), and to other similar circumstances. When Haller and Soemmering report that this disease is strikingly frequent among the prisoners at Cassel and Mayence, we should certainly be inclined to assign the lack of exercise as the principal ground for this, although a deficiency of light and air, improper nourishment, and other causes, may contribute toward it. Glisson[1] was one of the first to demonstrate that cows often suffer with gall-stones during the winter, when they are fed on hay and straw, these stones passing from them in the spring when they feed on grass. We will not pretend to decide whether, as Frerichs claims, this is due to their rest in the stall during the winter and their more abundant exercise in the meadows in spring. Probably the method of diet and the lack of exercise co-operate to this end.

9. Any *anatomical changes* in the liver and gall-ducts which are calculated to *render the excretion of bile more difficult* favor the formation of gall-stones. To this class, among others, belong tumors which press on the biliary passages (for instance, cancer of the liver), or which are situated in the walls of the gall-bladder, inflammations and degenerations of the gall-bladder, as well as adhesions of the same to neighboring parts, by means of which changes the contraction of the bladder and the consequent evacuation of its contents is rendered difficult or even impossible. Everything that induces the blocking up or compression of the biliary passages becomes at once an indirect agent in the development of gall-stones, and those stones which arise within the gall-ducts are almost all to be referred to causes of this kind (for instance, phlegmonous inflammation of the ducts, etc.).

Finally, *catarrh of the gall-bladder* and of the *biliary passages* must still be mentioned as a prominent cause of cholelithiasis. In view of the so frequent coincidence of gall-stones and catarrh of the bladder, we have every reason to be cautious in judging of the causal connection between them, for it is evident that gall-stones may just as well give rise to the catarrh of the gall-bladder, etc., as, on the contrary, to be themselves caused by

[1] Anatomia hepatis, p. 105. Hogæ Comitum, 1681.

this catarrh. Although, in any individual case, the causal connection may not be plainly seen, yet this much is certain, that catarrh favors the development of stones in general, in the gall-bladder as well as in other cavities and canals lined with a mucous membrane. It is highly probable that the method by which catarrh of the biliary passages contributes to the development of biliary concretions is variable. By means of swelling of the mucous membrane in the ducts, by means of a semi-paralyzed condition of the gall-bladder, the catarrh may hinder the flow of bile. Or, again, a chemical alteration of the bile, especially the acid reaction of the latter, may be brought about by the excessive secretion of mucus which is mingled with the bile, and thus the formation of calculi is excited by chemical methods. Finally, the products of catarrhs, such as lumps of mucus and the like, may furnish the nucleus about which substances precipitated from the bile may collect and form a concretion.

10. *Foreign bodies*, which play so prominent a rôle in the formation of urinary and intestinal calculi, being met with so seldom in the gall-bladder or biliary passages, rarely give occasion to the formation of gall-stones. The few known instances of this kind have already been mentioned. We may, however, refer to the conjecture of Mettenheimer,[1] according to which shreds of the mucous membrane of the gall-bladder, which have undergone fatty or calcareous degeneration, when they have become detached, might serve as the nucleus of concretions.

Pathology and Pathological Anatomy.

Gall-stones may originate and grow wherever there is bile. They are therefore occasionally met with in all parts of the biliary passages, but no doubt their original development takes place only in the gall-bladder and in the bile-ducts of the liver. Whenever they are seen in other places they have undoubtedly travelled thither, by various ways, from the parts above named. The way indicated by nature leads through the excretory ducts of the liver or gall-bladder, finally evacuating all stones through the ductus choledochus communis into the intestinal canal,

[1] Archiv f. Anat. u. Physiol. von Reichert u. Dubois-Reymond. 1872, p. 509.

whence they then usually escape per anum, rarely travelling upward. Exceptionally, though much oftener than is generally believed, stones leave their original place of development by unnatural paths, opened by means of ulceration and perforation, reaching various and often far distant parts of the body.

In the interior of the liver, and in the branches of the hepatic duct, gall-stones are comparatively rarely met with; still there are a good many observations to this effect on record from more ancient as well as modern times,[1] and every busy anatomist will be able to add to this number from the circle of his own experience.[2] Sometimes we find the ducts of the liver, throughout their entire extent and down to their finest branches, stuffed with an immense number of concretions, which are generally small and black, and often soft. Sometimes we find, principally in the larger hepatic passages, a moderate number of brown, irregularly angular stones, with facets, ranging from a size above that of a cherry-pit down to that of a millet seed. Again, we may find certain of the coarser passages filled, for a greater or less length, with cylindrical stones, nearly one centimetre thick. Even branched, coral-shaped concretions, solid or hollow, have been observed in the liver passages.

The bile-ducts are generally found dilated by the gall-stones, sometimes to a very high degree, up to two centimetres in diameter. The dilatation is usually uniform; rarely it is sacculated, the concretions lying in niche-like projections of the wall of the duct. Calculi, furthermore, cause an inflammatory irritation of the walls of the ducts, which sometimes results merely in catarrh, with an abundant secretion of mucus, sometimes leads to ulceration and purulent destructive changes in the duct walls, but more frequently terminates in proliferation of connective tissue, and considerable thickening of the walls of the ducts in the shape of weals. The inflammation set up by the gall-stones may also extend to the neighboring glandular tissue, which is thereby thrown into a state of cirrhotic induration, in fact may be com-

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[1] *Morgagni*, De sedibus, etc., epist. 37, art. 11. *Fauconneau-Dufresne*, l. c., p. 153 et seq.

[2] Compare the pictures in *Cruveilhier*, l. c., livre 12, pl. 5; in *Lebert*, l. c., pl. CXXV., fig. 6.

pletely obliterated for a certain distance. Liebermeister[1] describes such a case of interstitial hepatitis, in consequence of gall-stones, which filled the biliary passages of the liver. If the inflammation set up by the gall-stone assumes an acute character, purulent destruction of tissue follows, and we have an abscess of the liver. In our part of the world probably the majority of the cases of idiopathic hepatic abscess originate in this way. If the inflammation extends from the bile-duct to the branch of the portal vein accompanying it, then a pylephlebitis is developed.

Sometimes gall-stones are found in the liver, enclosed in a cyst-like connective-tissue capsule, which do not lie within the biliary passages, but appear enclosed on every hand by liver parenchyma. This state of things might be most naturally explained on the theory that the stone originally contained in the biliary canal had caused adhesive inflammation resulting in the obliteration of the canal and the formationof an enclosing capsule about the concretion. Pierquin[2] has seen a pure cholesterine stone of the size of a pigeon's egg within a hard, thick-walled connective-tissue capsule in the midst of the liver parenchyma ; also a second stone of the same kind as large as an almond in a similar capsule.

The *hepatic duct* itself is more rarely the seat of concretions than any other portion of the biliary apparatus. This is easily explained. For, as a rule, stones that reach the hepatic duct have come thither from the branches of this canal within the liver. The further these stones advance, the wider the canal grows ; therefore, as a rule, they are not retained in the hepatic duct, but pass on into the common duct. We cannot determine

[1] Beitr. z. pathol. Anat. u. Klinik d. Leberkrankh. Tüb., 1864, p. 135. Similar observations, although they are assailable on the point of the supposed causal connection, are reported by Fargstein (Berlin. klin. Wochenschrift, 1877, Nos. 16, 17, 19), and by Roller (ibid., 1879, No. 42). I once saw, on the sharp border of the left lobe of the liver of an elderly person, a sharply defined portion of the organ, about a cubic inch in size, covered by peritoneum thickened in weals, where the glandular tissue had disappeared to the last trace, and where the sacculated, distended bile-ducts were filled with cylindrical, knobby stones and mucus. Between the thickened walls of the canal there was but a little connective tissue.

[2] Cited by *Fauconneau-Dufresne* (l. c.), p. 156.

whether stones which originate in the gall bladder and have passed through the cystic duct can ascend into the hepatic duct. Such a performance must certainly be extremely rare. The autochthonous appearance of concretions within the trunk of the hepatic duct can hardly be supposed to take place unless the canal is the seat of irregular dilatations or other deformities favorable to the stagnation of bile and the development of stones. The few cases of stones in the hepatic duct have presented very varied conditions. In one case we may find a stone freely movable in the canal without its being apparent just what should retain it in this place. In another case, especially when the stones are larger, they are wedged tightly within the duct, and if they remain in this position long, a correspondingly wide dilatation of all the biliary passages must result, as well as a stasis of bile. It is, of course, to be expected that stones which are retained within the hepatic duct, especially if they are wedged in there, should induce catarrh, ulceration, etc., of the walls of the canal. In other cases, again, calculi accumulate within the hepatic duct, because the common duct is likewise filled with the same, whereby the escape of stones within the hepatic duct is rendered impossible. Cruveilhier's case (Atlas, livr. XII., pl. 5), already cited, was of this sort, the entire biliary apparatus being filled with blackish green stones, the hepatic duct, as well as the other canals, being greatly dilated, the bile, at the same time, flowing down into the intestine alongside of the stones.

The *gall-bladder* is the place where gall-stones are developed most frequently and in the largest number, for here they find the most favorable conditions for their formation. The spatial relations between the gall-bladder and the concretions it contains, vary very much according to the size, shape, number, and other conditions of the latter. Generally the stones lie free and movable within the bladder; they are often surrounded by healthy bile, and the bladder itself shows no pathological change whatever. In rare instances the calculi lie in diverticula of the cystic wall, for the formation of which they have probably themselves given the first occasion. Sometimes, also, firm concretions of coloring matter, from the smallest size up to that of a millet-

seed, are found embedded in the substance of the mucous membrane of the bladder, with regard to which it is supposed that they were originally developed in the dilated gland cavities of the mucous membrane.[1] Occasionally firm adhesions exist between a larger stone and the surface of the mucous membrane, so that the stone is with difficulty loosened from its attachment to the organ, or the concretion may be partly or entirely enclosed in newly formed connective-tissue membranes which adhere firmly to it.[2] The more extensively the stones lie in constant contact with the mucous membrane of the bladder, and the more rough and uneven their surface, the more surely will they call forth inflammatory changes in the mucous membrane as well as in the entire wall of the gall-bladder. Either a catarrh of the mucous membrane ensues, the latter is swollen and injected, secreting mucus and pus from its free surface, which are mingled with the bile as long as the cystic duct remains permeable; or ulceration occurs, ulcers of larger or smaller size being developed, or sometimes even the entire mucous membrane presenting one continuous ulcerated surface. The ulcerative loss of substance sometimes affects only the upper layers of the mucous membrane, sometimes its entire thickness, or, finally, the ulceration, softening, and necrosis may extend to the other coats of the gall-bladder and end in perforation of the bladder.[3] The

[1] This circumstance was known to *Morgagni*. Of late *Frerichs*, *Gubler*, *Durand-Fardel*, and others have made similar observations. It has been assumed by others, no doubt unjustly, that the concretions in question originally arose within the cavities of the biliary passages, and that they had tried to perforate the walls of the latter and stuck fast in the attempt.

[2] I recently found the gall-bladder of an old woman filled with a large number of stones, two of which, of the size of a walnut, and barrel-shaped, lay next to the neck of the bladder, while the rest, of the size of a pea, and having facets, completely filled the body of the organ. Every one of these stones, even those which did not touch the walls of the bladder, was enclosed in a separate chamber, formed by bands and cords of connective tissue given off by the mucous membrane, whose surface was smooth and cicatricial, these bands occupying the space between the rounded edges of contiguous stones. These dividing walls passed like lattice-work through the entire width of the cavity of the organ. The individual chambers stood in open communication with one another by means of round orifices corresponding to the facets of the stones. There was no trace of bile nor of mucus in the bladder, the cystic duct was obliterated, and the thin wall of the organ consisted of a simple layer of indurated tissue.

[3] Compare the section on Cholecystitis, etc.

further fate of the patient in that case depends on whether, at the moment of perforation, the gall-bladder is or is not grown fast to neighboring organs. In the first case it results in the formation of a biliary fistula (which see); in the other, in the escape of bile, perhaps also of the stone itself, into the cavity of the abdomen. The latter is especially liable to occur when the stone, by pressure on the otherwise round bladder, causes a gangrenous softening of the same. With regard to the results of this occurrence, which, as a rule, consist in a rapidly fatal peritonitis, compare the chapter on Ruptures and Perforations of the Biliary Passages.

Occasionally the ulcers heal again, although sometimes the gall-bladder remains filled with stones as before. Radiate, smooth, whitish cicatrices are formed, which contrast sharply with the reticulated appearance of the normal portions of mucous membrane.

Another class of cases is characterized by the fact that the stones contained in the gall-bladder beget a chronic state of inflammation of the walls of the latter which results in the atrophy, and finally in the complete devastation of the bladder. In these cases both catarrhal and ulcerative changes take place simultaneously on the surface of the mucous membrane, but at the same time a chronic *phlegmonous* inflammation of the mucous membrane occurs which leads to diffuse connective-tissue proliferation. The mucous membrane then assumes a more smooth, uniform surface, a whitish appearance, and a leathery, tough quality. The bladder also draws itself firmly about its stony contents, which is particularly the case with very large, solitary stones. By reason of its constant efforts to rid the organ of its abnormal contents, the muscular coat of the bladder undergoes well-marked hypertrophy and assumes a more flesh-like character. This hypertrophy is not always uniform, but sometimes particularly affects certain fasciculi of muscle. These, then, stand out more prominently on the inner surface of the gall-bladder and, under some circumstances, lend this surface an appearance similar to what is seen in that form of hypertrophy of the urinary bladder known as *Vessie à colonnes*. If stronger bundles of muscular fibre stand out singly, and it hap-

pens that a stone lies between them, the walls of the bladder may sometimes, by this means, be pouched like diverticula; or, in case the hypertrophied muscular bundles run in a circular manner, the organ itself may be divided into several successive compartments communicating with one another. The serous covering of the bladder likewise takes part in the inflammation; it becomes thickened into a whitish rind, and forms adhesions, sometimes by means of loose cellular tissue, sometimes by tense fibrinous masses with neighboring organs, especially with the transverse colon, the duodenum, the stomach, etc. The concretions, tightly enclosed by the thickened bladder-walls, now constitute the sole contents of the gall-bladder. There is no room left for bile; as the mucous membrane has grown smooth and exchanged its original anatomical character for that of a thickened serous membrane, no mucus nor pus is any longer produced, and the inner surface of the bladder often seems inseparably adherent to the outer surface of the stone. Finally, a retrograde metamorphosis may be set up in the tissues of the gall-bladder in such a way that the muscular coat atrophies and the entire walls are transformed into a rigid shell almost as hard as bone by means of the deposits of lime salts. Thus the typical end of the process is reached, the stone is encapsulated, the bladder completely destroyed. This condition remains stationary to the end of life. The stones in the bladder have thus become entirely harmless.

While, on the one hand, those changes are taking place which tend toward the devastation of the gall-bladder, some ulcer may, on the other hand, penetrate into the depths of the mucous membrane and cause perforation of the organ with the results previously indicated.

Although gall-stones often enough cause serious disturbances by their sojourn in the gall-bladder and the ducts of the liver, yet in most cases the series of pathological manifestations does not begin until the concretions are set in motion in order to leave their place of origin by one route or another. This change of location may take place in one of two ways. The gall-stones, in their wandering, may take the route prescribed by nature, passing out of the gall-bladder through the cystic into

the common duct, or from the ducts of the liver direct into the latter, then forcing themselves through the diverticulum Vateri into the duodenum, to be expelled through the mouth or, as a rule, through the anus. Or, again, the change of location may be effected by means of unnatural routes, the concretions giving rise to ulcerative processes by means of which they are at least enabled to forsake their original location, and are also often finally expelled from the organism (by so-called biliary fistulæ). In either of these ways the cure of cholelithiasis may be accomplished—that is, the complete removal of gall-stones from the body. But the process of a change of location itself is very often associated with the greatest suffering and danger to the patient.

So far as the passage of gall-stones by the natural route is concerned there is no trouble in understanding how they may be transported from the ducts of the liver into the ductus choledochus, but the same cannot be said with regard to the entrance of stones from the gall-bladder into the cystic duct. If the ducts of the liver interpose no special hinderance to the movement of calculi, if the latter do not lie in pouches of the ducts, are not grasped with unusual force by the walls of the latter nor adherent to the same, if the stones do not possess a diameter disproportionate to the normal calibre of the passages, then, as the system of canals increases a little in width till near the mouth of the common duct, we can readily understand how the current of the bile should suffice for the transportation of the calculi until they reach the diverticulum Vateri, especially if the current sometimes becomes stronger under a temporary increase in the amount of bile, and inasmuch as this movement is also aided by an appropriate position of the body and, perhaps, also by the action of abdominal pressure.

We have, however, no clear insight into the mechanism whereby calculi pass from the gall-bladder into the neck of the organ and the cystic duct. Although the advance of stones into this duct may depend upon various causes, we cannot but admit that the stream of fluid which is pressed out of the gall-bladder occupies the first place among these causes, and is indispensable thereto. The stone is, so to speak, caught by a wave

and thrown by it into the neck of the bladder. Aside from the contraction of the organ itself, certain adventitious circumstances may contribute to render the propulsion of the bile more powerful, as, for instance, abdominal pressure (at stool), acts of vomiting, certain positions of the body, perhaps also external influences, as blows upon the abdomen, etc. The supposition that a powerful current is necessary for this purpose is supported by the observation of Willemin, who repeatedly found that attacks of hepatic colic were *preceded* by an unusually great fulness of the gall-bladder. If the bladder then contracts powerfully to relieve itself of its fluid-contents, one or more concretions may be seized by the current and driven into the neck of the organ. Patients, it is true, generally blame an attack of indigestion as the occasion of the paroxysm of biliary colic. Even if they should be right about this, it would not help us to understand the entrance of the stone into the duct; and, on the other hand, it might with justice be asserted that the (latent) beginning of a paroxysm, if it happened to coincide with the process of digestion, might cause all sorts of disturbances of the latter.

The anatomical relations of the cystic duct are by no means favorable to the progress of the stone toward the common duct. Larger concretions, or those which are unfavorably situated, are often retained even in the neck of the bladder, while others, even tolerably small ones, of not more than 3 to 4 mm. in diameter, are frequently arrested within the cystic duct. The sharp bend in the canal immediately behind the neck of the bladder, its average normal width of only about 3 mm. in diameter, the fold-like projections of its wall in the direction of the lumen,—all these factors contribute to render the passage of stones through the cystic duct difficult. Inasmuch as the cystic duct itself possesses no muscular fibres, the only thing that can serve as a propelling power is the *vis a tergo* which the bile following it, driven by the contraction of the muscle of the bladder, exercises upon the stone.[1] To what extent the propelling power of the bladder is supported by abdominal pressure, by the respiratory

[1] The influence which the muscular coat of the bladder exercises on the process in question is proved by those cases where hypertrophy of its muscular bundles has been developed after the analogy of the *Vessie à colonnes*.

movements and other influences, cannot be even approximately estimated. We shall return to the question of how large a stone may be and still pass through the cystic duct, when we discuss the passage through the still narrower diverticulum of the common duct.

The time required to pass through the cystic duct varies within very wide limits for stones of different sizes, etc. The only basis given us for determining this question consists in the duration of paroxysms of biliary colic (see below). Many stones never pass through the duct. They become *tightly wedged* between its walls and remain there permanently, if they are not afterward released from this position by ulcerative perforation, which happens very seldom. Gall-stones imprisoned within the cystic duct generally close its canal completely, so that the entrance or escape of bile to or from the bladder is entirely arrested. This gives rise to what is called dropsy of the gall-bladder (which see). Aside from this, the retention of stones for a considerable time in the cystic duct probably always leads to inflammation of the walls, or at least of the mucous membrane of the duct, the most important results of which are the organic closure of its lumen (adhesive cholangitis), and ulcerative perforation of the duct (compare the section on Cholangitis and on Perforation of the Biliary Passages). Even when a stone which has been retained in the cystic duct for some time finally does pass into the ductus choledochus, the inflammation caused by it may lead to the narrowing or to the obliteration and wasting of the former.

Concretions which have advanced as far as the ductus choledochus meet their last and greatest hinderance at the narrowest point of the entire passage, viz., at the diverticulum Vateri. They advance with their anterior extremity quite in the neighborhood of the opening, they can sometimes be seen from the intestine with their point projecting into it, but are then, for the time being, held back by the walls of the canal terminating in funnel shape. According to the size and shape of the stone present, as well as the dimensions of the canal, the following alternative arises: either the stone is everywhere so closely surrounded by the walls of the canal that not a drop of bile can

flow past, and stasis of bile must follow (if this close imprisonment does not exist from the first, it may be brought about sooner or later through the inflammatory swelling of the mucous membrane caused by the irritation of the stone), or the calculus still possesses a certain mobility, is not everywhere tightly enclosed, and the bile can flow past it, even though it be in but a feeble stream, and enter the intestine. The first situation carries in itself the conditions for its relief, for the stasis of the bile is finally the means by which the stone is completely driven through the diverticulum.

If, now, we look for the propelling forces which are capable of accomplishing this, we shall find that the only one of importance is the pressure of the bile from behind. For the ductus choledochus is almost entirely deficient of any muscular elements such as are found in the intestine and the ureter, and which might push the contents of the duct forward. Abdominal pressure, however, cannot develop its power properly unless a larger amount of fluid is accumulated in the biliary passages; and furthermore, it can only exert its influence in the propulsion of the stone so long as the patient is not prevented by pain from permitting it to act. So far as the pressure of the bile is concerned, the amount of pressure exercised by its secretion, and which, under ordinary circumstances, causes the flow of this fluid, is certainly but slight. But this pressure of the fluid in its canals is manifestly increased through the stasis of the bile, caused by the stone closing the diverticulum, and which, if it lasts long enough, leads to jaundice. If now the increased tension of the walls of the biliary passages has added to it a powerful contraction of a very full gall-bladder, heightened by the action of abdominal pressure, which the patient may instinctively increase by closure of the glottis, etc., we readily see that all these circumstances tend to the dilatation of the diverticulum, which will finally reach a point that admits of the escape of the stone. The degree of pressure at which the pent-up bile, in its passages, may stand is best demonstrated by the fact that it is sufficient to cause a rupture of its excretory duct when this is otherwise in a perfectly normal condition.

It is, of course, also evident that certain limits are set to this

process of expulsion by natural means. What these limits are, in other words, to what size the diverticulum is ever dilated, or how large a stone may be able to pass this part, is a question about which there has been much strife; and it would be a hard matter to-day to answer definitely, that is, to determine a fixed dimension which a stone may not surpass, unless it is to be inevitably doomed to retention behind the diverticulum.

In discussing this question, there has been a great lack of the necessary criticism. Some have been satisfied with the idea that every stone, great or small, which has traversed the intestines has reached there without leaving the natural route of the biliary passages, unless the contrary was expressly demonstrated. And yet, in the case of large stones, especially if they have passed *without* the symptoms of biliary colic, without severe pain, jaundice, etc., the presumption exists from the outset that they have arrived in the intestine by some other than the natural and far too narrow way. For in general it must certainly be taken for granted that the larger the stone, the more severe will be the symptoms accompanying its passage through the cystic duct and the diverticulum of the ductus choledochus. Experience, however, teaches that large gall-stones are the very ones which often produce no serious disturbances until they are in the intestinal canal, while their passage thither from the gall-bladder may have been quite unobserved. It is evident that under such circumstances these stones cannot have reached the intestine by the natural channels.

The question of how large a stone may be in order to be able to pass the diverticulum cannot therefore be answered according to the size of concretions evacuated per anum, but the answer will have to be based on the measurement of those stones which are demonstrated to have been permanently retained in the duodenal extremity of the ductus choledochus. According to all that I have myself seen on the post-mortem table, and which I can gather from reliable observers, I believe that a gall-stone of about one centimetre in diameter is the largest that can ever pass the diverticulum. For the majority of cases, however, even this measurement is probably too high, as much smaller stones than this have been found wedged into the ductus choledochus, or at

least permanently retained there. In my opinion, therefore, it would not generally be easy for a stone to pass the diverticulum with a diameter of more than about seven or eight millimetres.

If, on the whole, stones of this size are seldom found imprisoned behind the diverticulum, this may be accounted for on the ground that they are also too large to pass from the gall-bladder into the cystic duct. If, nevertheless, much larger stones are occasionally found in the common duct, which certainly do not always come from the liver ducts, but sometimes from the gall-bladder, we must remember the possibility that such concretions may have reached the size which they present at the autopsy during their sojourn in the ductus choledochus. An unprejudiced observer cannot fail to see that some stones of this sort present unmistakable evidences of such growth during the period of their retention.

The second one of the two alternatives indicated by us above is that the stone may remain lying loose in the duodenal extremity of the common duct, or at least, by reason of its peculiar form, may not be so tightly grasped on all sides by the walls of the canal but what the bile can flow down alongside of it. Under these conditions no stasis of bile can be developed; consequently, the only effective driving power which might move the stone forward is lacking, and it remains in its place; the symptoms of biliary colic, paroxysms of pain, jaundice, etc., are absent, or at least appear in a very light form. But even here a change may occur with time; for, in the first place, the stone may continue to grow until it completely fills the diameter of the passage, and secondly, it may occasion an inflammatory swelling of the mucous membrane, so that the canal now tightly encloses the stone. As soon as this moment has arrived, all those conditions go into effect which have been described under our first alternative.

With larger stones, which have been long retained in the ductus choledochus, we must distinguish whether they are wedged in or lie there loose. In the first instance all the results of closure of the common duct would set in—chronic jaundice, dilatation of all the biliary passages, finally dropsy of the same, atrophy and degeneration of the liver, parenchyma, etc. During the

first period of the closure, perhaps for a number of months, attacks of colic occur from time to time, which, if they become very severe, may lead to rupture of the bile-duct (which see). Generally, however, these attacks diminish gradually in intensity, the intervals between them are increased, and finally they cease altogether. If stones lie loose in the duct, no evidences of closure will appear, or they will be transitory and mild in degree. Calculi which are wedged into the duct, as well as those which are loose, though especially the former, maintain a catarrh of the duct, which may lead to ulceration and perforation, and by good fortune may even result in a change of location of the stone, with its final expulsion and the disappearance of the jaundice, which has until then been permanent.

Sometimes the ductus choledochus is found distended into a wide sac, which contains numerous stones, while the flow of bile into the intestine is not interrupted (compare the illustration by Cruveilhier, Atlas, livr. 29, pl. 4, fig. 3). Morgagni reports a case where the duct was dilated in bottle-shape, and found full of stones. And we have already above referred to an observation of Frerichs, in which he saw the common duct transformed into a sac eight inches in length by five in width.

We now come to speak of the changes of position and of place which stones undergo through *unnatural routes*, by means of ulcerative *perforation*, more rarely by means of rupture of the biliary passages (which see). Although less frequent than the passage through the biliary canals, it is still not as infrequent an occurrence as is believed by many. Stones of every size, form, and composition, and originating at any point, are capable of such a change of position. It is only necessary to suppose that they lie in sufficiently close contact with the wall of the bile-duct to induce ulceration or gangrene of the same. The direction which stones take, and the more immediate circumstances under which the change of place is accomplished, vary very much. The following ways of escape are especially to be noticed :[1]

[1] Compare the section on Biliary Fistula. *Murchison* is entitled to the credit of having collected the cases in question. In the second edition of his Diseases of the Liver (1877) he counts among his own observations, and those of others, twenty-eight duodenal fistulas, seven of the colon, four gastric, and seventy of the skin.

1. Stones pass through fistulas from the gall-bladder *into the stomach*. This has been seen but seldom. Murchison (op. cit., p. 497) only adduces four fistulas of this kind caused by gall-stones, two of which are said to be mentioned by Frerichs,[1] though I have not been able to find them in his Klinik der Leberkrankheiten. Cruveilhier (Traité d'anat. pathol. II., 541) observed such a fistula, in which a gall-stone was found enclosed. Oppolzer (Zeitschr. d. Ges. d. Aerzte in Wien, Nov., 1860) found such a fistula in a man thirty years old, which opened into the stomach close to the pylorus.

2. Gall-stones more frequently pass from the biliary passages into the intestinal canal through fistulas that open *into the duodenum*. With rare exceptions such fistulas are always caused by gall-stones. Murchison has collected thirty-four cases of this kind, a number which could easily be increased. It is worthy of remark that, in the majority of these cases, death followed from closure of the intestinal canal through unusually large gall-stones which had passed through the fistula. But inasmuch as stones which have passed through a fistula may also escape per anum, and the patient long outlive the process, it is probable that such fistulas often heal up again, so that the traces of them might easily be overlooked in a post-mortem. This would argue in favor of the probability of the development of fistulas between the biliary passages and duodenum—that is, the passage of gall-stones by this route, as being far more frequent than has generally been supposed. The entrance to the fistula generally corresponds to the fundus of the gall-bladder; more rarely it occurs at the ductus choledochus. Its outlet, according to Murchison, lies, as a rule, in the lower horizontal portion of the duodenum. The width of the fistula varies according to the size of the stone that has passed through it, and the length of time that has elapsed since the passage of the stone, for it grows gradually smaller. In some cases, as already remarked, there is doubtless, at last, complete obliteration of such fistulas.

3. It is comparatively rare for stones to pass by a fistula that

[1] Klinik d. Leberkrankheiten, II., p. 506. All that is said here is: "Baillie and Weber mention a fistulous communication between the gall-bladder and stomach, which they considered congenital."

opens *into the colon.* This difference, as over against the duodenum and the biliary fistulæ opening into it, evidently depends upon the greater mobility of the colon. Murchison (op. cit., p. 499) found only nine cases of this variety of fistula, including those of his own observation, and six of these were cancerous fistulas, leaving but three caused by gall-stones alone. One case, the preparation of which is preserved in the collection of St. Bartholomew's Hospital, is remarkable; here there are two fistulas, one leading into the small intestine, the other into the colon.

A large stone had passed through the first one into the ileum, another, equally large, through the second into the colon, and was found in the cæcum. Murchison (l. c., p. 499) gives a case similar to this where three fistulas led respectively to the duodenum, the colon, and the external skin. As there was no cancer, it was to be supposed that the cause of these fistulas consisted in gall-stones which in the meantime had been expelled. But even where there are fistulas due to cancer, gall-stones have usually aided in their production. Among the six cases of cancerous fistula mentioned above this was demonstrably true in five.

4. Concretions from the gall-bladder may also wander *into the urinary passages* and be evacuated with the urine. The three cases of that kind which have thus far been observed are recorded on page 662. In only one of them (Faber-Koestlin) did the post-mortem examination demonstrate the route taken by the gall-stone. The fistula led from the gall-bladder to the neighborhood of the umbilicus, and here communicated with the open urachus, through which the stone descended into the bladder. The route which Fauconneau-Dufresne and Murchison suppose to be taken from the gall-bladder into the pelvis of the right kidney would, indeed, be the most direct in a topographical point of view, yet no one has really ever seen stones pass into the urinary tract by this way. In the Faber case the patient, a woman, thirty-five years of age, passed urine containing bile (without ever having icterus, though the fæces were sometimes pale), and in the course of three years passed nine smaller and four larger gall-stones with her urine, sometimes requiring mechanical assistance to pass them through the urethra. With

the expulsion of the last stone the normal condition of the urine and fæces was restored, as well as the general good health of the patient. No gall-stones were ever found in the stools. The smaller stones weighed about half a gramme, the larger fully 2.5 grm. As they consisted of cholesterine, the larger ones must have been as large as a small cherry.

The second case (Barraud-Pelletan) was also in a woman about thirty-seven years old, who had suffered much from migraine and bilious vomiting. Urinary troubles set in; after these had lasted two months about two hundred little stones of the same composition as those in the other case were spontaneously evacuated with the urine. A month later a larger stone was arrested at the neck of the bladder, and its escape had to be facilitated by the pressure of the finger introduced into the vagina. Hereupon the urinary troubles and the passage of stones ceased, and good health was restored. The weight of the stones was from 0.5 to 2.6 grammes; they consisted of 95 per cent. of cholesterine, and had facets. The urine never contained bile, and there were, in fact, never any symptoms of cholelithiasis.

In the third case (Gueterbock) urinary troubles, consisting of frequent and painful urination, were set up without any apparent cause in a previously healthy woman, fifty-seven years old. After this had continued for six months three stones were evacuated with the urine after severe straining. Some time after several stones of almost the size of a walnut were crushed within the bladder with Luer's forceps, at four sittings, and the fragments evacuated with the urine. Since that she has been well. The assembled fragments of stones weighed 13 grammes, and consisted in the main of cholesterine. Here, also, there were no other signs of cholelithiasis.

5. Gall-stones, even of large size and several in number, have occasionally been found *in the interior of the portal vein*, although it has not always been possible to find any communication between the biliary passages and the portal vein. In former times it was therefore assumed that such stones were developed in the portal vein itself out of diffused bile, and this was very natural in view of the knowledge of our predecessors concerning the functions of the liver. It requires no argument to-day to

prove that this is impossible. The only possibility remaining is that the gall-stones reach the portal vein by means of ulceration and perforation. We will not here inquire any further as to what the more immediate methods of this process may be. The oldest observation of this kind dates from Realdus Columbus, who is said to have found three gall-stones in the portal vein of Saint Ignatius Loyola.[1]

Jacob Camenizenus[2] describes the case of a man who had long suffered from icterus and afterward from dropsy, and the branches of whose portal vein were said to be quite filled with stones that were black without and yellow within. A similar stone was found in the ductus choledochus. If one were disposed to challenge the two observations just cited, this cannot be done with the following cases reported by quite reliable observers.

Deway,[3] physician to the Hôtel-Dieu in Lyons, made an autopsy on a woman forty-seven years of age, who, seven years be-

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[1] In *Frerichs* (Klin d. Leberkrankheiten, II., 507) it is added that the stones in question had made a way for themselves from the bladder into the trunk of the vena portæ. I cannot see where *Frerichs* got this idea. *Bianchi* (Histor. hepat., Genevæ, 1725, p. 191), whom *Frerichs* quotes in support thereof, says: "Finiamus . . . . observatione *Realdi Columbi* qui Romæ in ipsamet venæ portæ cadaveris Sancti Ignatii tres calculos biliosos invenit; ut habetur ex vita ejusdem sancti: Adeo jam. biliosa corpora, in tophos ulterius concrescibilia, per ipsammet portam arcte coadunata jam sunt, ibidemque ante secretionem hepaticam a toto sanguineo distincta et secreta. Ut in prima parte hujus historiæ fusius probavimus." From these tolerably obscure words one might, at need, draw the conclusion that the origin of the gall-stones was supposed to arise from bile diffused in the vein. Whether the stones in the portal vein of Saint Loyola were really gall-stones or ordinary phleboliths, as *Thudichum* thinks, must remain undetermined.

[2] *Phœbus*, De concrementis venarum osseis et calculosis. Berol., 1832, p. 44. We agree with Phœbus, who assumes that the stones in question did not lie in the branches of the portal vein, but in those of the hepatic duct. It is a matter of indifference to us whether Camenizenus took those concretions to be gall-stones or ordinary phleboliths (compare *Phœbus*, l. c.).

[3] Gaz. méd. de Paris, 1843, No. 17. Communicated in extenso by *Fauconneau-Dufresne* (op. cit., p. 342), in outline in Schmidt's Jahrbb., 1844, Heft 3, and in *Frerichs* (l. c., p. 507). *Deway* also reports (*Fauconneau-Dufresne*, l. c., p. 340) that one of his colleagues at the Hôtel-Dieu in Lyons, Dr. Imbert, assured him that he had encountered a large number of small stones in the interior of the portal vein. There are no further particulars about this, nor were the stones analyzed.

fore, had suffered from intermittent fever for six months. Of late she had suffered from jaundice with alternate constipation and diarrhœa. The liver was found diminished in size, of a yellowish green color, and soft. The trunk of the portal vein was at least twice as thick as the inferior vena cava. In the right branch of the portal vein, just where this penetrates the liver, there was a stone of something over 2 ctm. in length and 4.1 grammes in weight. Deep within the parenchyma of the liver, in the branches of the portal vein, there were little cylindrical calculi similar to the large one in the right branch. The gall-bladder, completely devastated, contained a stone of the size of a small nut, weighing 3.20 grammes. The cystic and common ducts were completely obliterated and transformed into thin, fibrous bands. The large stone in the right branch of the portal vein was easily broken, black without, brown within, and its centre darker; it consisted of concentric layers strewn with little crystalline granules. Its principal component was cholesterine. Aside from this, it contained stearine, coloring matter, resinous components, picromel, and salts of magnesia.

Another case was observed by Murchison[1] (l. c., p. 521). This referred to a woman fifty-seven years old, who suffered from cancer of the stomach, the pancreas, the liver, etc. The anterior margin of the liver was united to the pyloric extremity of the stomach and the pancreas by means of a large, nodular mass of cancerous growth. The tumor occupied the place of the gall-bladder and extended to the hilus of the liver. The portal vein and hepatic duct passed through the growth. The hepatic duct seemed to have remained pervious. But the portal vein, about an inch from its point of entrance into the cancer, was dilated into an irregular cavity whose ulcerated walls enclosed an oval gall-stone of about half an inch in its longest diameter. The cavity was closed, except so far as the openings of the venous branches were concerned. Beyond this point there was phlebitis of the branches of the portal vein, which were filled with partially softened clots. In the liver itself there were several abscesses in process of development. Unfortunately, no particulars are given with regard

[1] Bristowe's case, mentioned at the same place, has nothing to do with gall-stones.

to the relations between the hepatic duct and this collection within the portal vein.

So far as I know, no instance has ever been observed of the passage of gall-stones into the cavity of the pleura or into the air-passages, although fistulous communication between the biliary passages and the pleural cavity, or even the bronchi, has been seen in a few cases (see Vol. XXVIII., p. 157, Path. Trans.).

6. Sometimes gall-stones pass from the biliary passages into the *cavity of the abdomen*, through rupture or perforation of the former. This may happen with stones which lie within the gall-bladder, setting up ulceration and causing perforation of the same before the organ has become firmly enough attached to the neighboring parts; or it may happen with stones which have been arrested within the ductus choledochus and which, by arresting the flow of bile, have caused so great a distention of the duct as to rupture it without its being ulcerated or otherwise altered, thus permitting both the bile and the impacted gall-stone to escape into the abdominal cavity. Cases of this kind have been described by Pigné and Marjolin (Bull. de la soc. d'anat., 1836, 1837) among others. Gall-stones that have been impacted in the cystic duct seldom enter the abdominal cavity by perforation. In all such cases death generally ends the scene after a short interval of one or two days, as in other forms of peritonitis from perforation.

Another condition to be ranked alongside of those just mentioned is that in which stones that have perforated the walls of the biliary passages do not pass direct into the abdominal cavity, but into a sort of abscess filled with bile, pus, ichor, etc., the walls of which are formed by the adherent neighboring organs, and the cavity of which, though sometimes situated far from the liver, is in open communication with the gall-bladder. The stones that lie within such cavities may, under some circumstances, be expelled through the walls of the abdomen, the abscess being either artificially opened or spontaneously breaking through these walls at some point.

It has also occasionally been found that stones, especially those of smaller dimensions, after they have perforated the gall-bladder, have been enclosed between peritoneal pseudo-mem-

branes and ligaments, and have remained there undisturbed in the future. (Compare the case of Coupland in Pathol. Transactions, XXVIII., p. 157.)

7. Finally, gall-stones are expelled through *fistulas* penetrating the abdominal walls. With regard to these cutaneous fistulas we refer to what has been said before (p. 664). Up to the year 1877 Murchison (l. c.) had seen eighty-seven such cases. Their number, including those of Murchison, as well as the most recent observations, could easily be brought up to over one hundred. The expulsion of gall-stones through fistulas in the abdominal walls has taken place almost exclusively in women. The number of stones expelled through such a fistula varies from a single stone to several hundred. When only one stone has been expelled, this has repeatedly been of the size of a hen's egg, and might therefore be regarded as a cast of the gall-bladder which it alone must have almost entirely filled. In Fauconneau-Dufresne, a stone which escaped in this way is described as being 3.15 inches long and 1.1 inch in its largest diameter. The evacuation of the stones sometimes takes place immediately after the formation of the fistula, or within a few days, sometimes at greater intervals of time, and occasionally a stone is expelled after a fistula has existed for years. Not infrequently one or another stone remains lying in sac-like diverticula of the fistulous track, or it obstructs the latter completely, and becomes impacted therein, an accident which occasions the most violent pain to the patient, and demands surgical interference. The impacted gall-stones must then be extracted, and, under some circumstances, this necessitates the enlarging of the fistulous canal, either gradually by means of sponge or sea-tangle tents, or immediately by incision of its walls. It is not necessary to insist that in all interference of this kind the greatest caution should be exercised.

I desire here to call attention to a circumstance nowhere discussed and which may possibly, in some cases, serve to explain how gall-stones, even of considerable dimensions, occasionally reach the intestinal canal without having passed the diverticulum of the common duct, and also without our being able to find the perforation by which they have arrived there, nor any traces of it. I have found that tolerably often *a sort of (sac-shaped) diverticulum occurs in the duodenum*, which stands in close topographical relations to the intestinal extremity of the

ductus choledochus. The appendages in question are *mucous membrane diverticula*, and therefore very thin-walled. They are situated immediately to one side of the point of opening of the ductus choledochus, or 1 to 1½ ctm. above the same. Their neck has about the diameter of a finger's breadth, sometimes still wider. The sac of the diverticulum, which at its neck sets out sharply from the walls of the duodenum, is generally roundish. Once I found it elongated in the form of a purse. Its size is very variable. The largest one that I have yet seen was as large as a small apple, and its neck as wide as a mark-piece or shilling. The wall of the larger diverticula lies close to the cystic duct without being generally adherent to it, and is usually covered with flabby lobules of the pancreas. As a rudiment of this diverticulum I often find at the portion of the duodenal wall in question a thin-skinned patch as large as a lentil, devoid of muscular tissue. This circumstance would seem to point to a congenital origin of the diverticulum, that is, to its development simultaneously with that of the intestine. I have not yet been able to arrive at anything definite with regard to the history of its development. These appendages are easily overlooked if the duodenum is cut open. It is only when it is filled full, or accidentally distended with gas, that they are to be recognized from without by palpation. In order to discover the slighter forms of this development, I tie the duodenum two inches above and the same distance below the opening of the ductus choledochus, and then blow air into it through the duct. Then the sac-like appendage is filled, if it is present at all, and by careful handling all the topographical relations of the appendage can be shown. As to the frequency of its occurrence, I found it no less than seven times among forty-five bodies that I examined consecutively for this purpose, the size of the appendage varying from that of a pea to that of an apple, the width of its neck from that of a lentil to that of a shilling. Besides this, I two or three times found the mere indication of a diverticulum in the shape of a thin spot on the wall of the intestine. The seven cases comprised three men and four women, varying in age from twenty to seventy years. Even though further investigation should show that these diverticula of mucous membrane in the duodenum are more rare, on an average, than would appear from this brief series of observations, still the diverticulum may sometimes happen to coexist with a retained stone in the common duct, and therefore, from this point of view also, this subject is worthy of the future notice of pathological anatomists.

It now only remains for us to follow the fate of those gall-stones which have reached the intestinal canal, whether it be in the natural way through the diverticulum Vateri, or by the unnatural path of a fistula between the biliary passages and the intestinal canal.

The regular way in which such stones leave the body is that they pass down the intestines and are voided with the stools per

anum. Generally all symptoms disappear as soon as the stones have passed the ductus choledochus, their passage through the intestines following without any inconvenience to the patient. But under some circumstances the passage of stones through the intestines is associated with all sorts of annoyances, and even with the most alarming symptoms. Severe colicky pains, vomiting, and great prostration are called forth by the stones during their sojourn in the intestinal canal—that is to say, during their progress through it, and until their final elimination. These manifestations only occur with larger stones, with regard to which we have already expressed our opinion that they reach the intestine through fistulas from the gall-bladder, an opinion which had already been emphasized by Virchow, among others, and quite recently by Fiedler.[1] This is also consistent with the fact that the larger stones often cause no serious inconvenience until they find themselves in the interior of the intestine, while their movement thither has been more or less unobserved; but, on the contrary, those stones which pass through the ductus choledochus give rise to the manifestations of biliary colic so long as they are retained within the excretory ducts, and then pass over the rest of their way to the anus unobserved.

From the observations collected by Fauconneau-Dufresne (l. c.) and others, it appears that gall-stones of the size of a pigeon's or even a hen's egg have been evacuated with the stools. Murchison (l. c., p. 492) cites a case in which two stones were passed by the anus, one of which measured $1\frac{3}{4}$ inch in length by $1\frac{1}{2}$ in thickness, while the other was almost two inches long. Hilton-Fagge (Pathol. Transactions, XIX., p. 254) showed two specimens of gall-stones passed by the anus, and whose diameter was $2\frac{1}{2}$ by $1\frac{1}{5}$ inches. Blackburn, in the *Lancet* of 1868, describes one of the largest specimens of this sort. The stone was $3\frac{3}{8}$

[1] *Fiedler* (l. c.) asserts outright, on the ground of post-mortem observations, "*that gall-stones are much oftener expelled and reach the intestinal canal through ulceration and perforation than by the pre-existing paths of the cystic and common duct;* that the former method of passage is the usual one, and that only small concretions can pass the normal ducts without an anatomical lesion."

Perhaps Fiedler goes too far in his assertion. We consider it as an established truth that the opponents of this view do not go anything like far enough in admitting the expulsion of gall-stones by means of perforation. In this connection we are reminded that Rokitansky believes that even stones of the size of a hen's egg reach the intestine through the natural biliary passages.

inches long by 1½ inch thick, and weighed 52 grammes. It is said to have passed by the anus without any special discomfort after the usual symptoms of cholelithiasis.

As a rule, gall-stones undergo no further changes during their stay in the intestinal canal. Sometimes, under the pressure of intestinal contractions, they may be broken into a number of fragments, especially if several stones chance to meet. But it would seldom happen that a number of stones would coalesce to form a single large concretion, the size of which should be a hinderance to its progress, and thus cause the symptoms of intestinal colic as given above. A case of this kind is reported by Puyroyer.[1] He observed the closure of the jejunum through a conglomeration of gall-stones, which accurately filled the calibre of the gut, being melted together into a cylinder, which afterward, on being dried, fell into several pieces.

If gall-stones increase in size within the intestinal canal, as has been claimed by several writers, we shall have to suppose that this is accomplished by the intestinal mucus, mingled with other contents of the bowels, being precipitated in firm layers on the surface of the stone. The agglomeration of several stones into one larger concretion, as in the case of Puyroyer, might be explained in the same way. The supposition that gall-stones grow in the intestine by the apposition of biliary constituents, particularly of layers of cholesterine, cannot be accepted as of general application, because the bile is not present as such, but chemically altered, that is, in combination with the ingesta ; besides which, the movements of the intestines would have a disturbing effect on the process of crystallization. This circumstance was pointed out by Cruveilhier. The growth of a stone within the intestinal canal by the apposition of biliary constituents could only take place on the supposition that bile was present in a free state. This might, perhaps, be possible if there happened to be dilatations of the intestinal wall like a diverticulum (see above, p. 735) situated in the neighborhood of the papilla duodenalis, in which bile might be gathered, and if the stone

[1] Dict. encyclop. des sc. méd., par Dechambre, IX., p. 389, 1868.

came to be deposited in the same diverticulum. But it seems to us as if the growth of gall-stones within the intestines had been more taken for granted than proved. The assumption seemed necessary in order to account for the presence of very large stones within the intestinal canal, too large to have been able to pass the ductus choledochus, and which observers were unwilling to admit had entered through a fistula, or at least were unable to demonstrate the latter.

The expulsion of gall-stones from the body *by vomiting* is very rare. Two cases of it are cited by J. L. Petit (Mémoir de l'acad. roy. de chirurg., 1743. Vol. 1), the stone, in one case, measuring two and one-half inches in length. Eight such cases are collected by Fauconneau-Dufresne (op. cit., p. 259). Jeaffreson (Pathol. Trans., Vol. XII., p. 129) saw a gall-stone of the size of a nutmeg vomited by a woman ninety-four years of age. In Miles' case (Lancet, Jan. 19, 1861) the vomiting of masses of sarcinæ ceased after two large gall-stones had been expelled from the stomach. The act of expulsion is generally preceded, for several days, by severe pain in the stomach, as well as violent and persistent vomiting. The number of the stones vomited, in any given case, varies; their size is almost always considerable. Sometimes only one stone is thrown up, sometimes several; in one case more than twenty were expelled. In another patient the vomiting of gall-stones took place at three periods, separated by intervals of several years. With regard to the method by which these stones arrive in the stomach, we of course first think of the antiperistaltic action by which the concretions might be passed backward from the intestine into the stomach. At the same time it is very doubtful, as to stones of considerable size, whether they really pass back through the narrow pylorus, since the easier way downward through the intestine is open to them. These and some other circumstances render it probable that the stones in question have reached the stomach directly through fistulas from the gall-bladder. In one case of Jeaffreson's this was afterward demonstrated by the autopsy (see British Med. Journ., May 30, 1868).

After they have arrived in the intestine, gall-stones may become *firmly impacted in the latter*, and thus give occasion to

prolonged intestinal obstruction.[1] The medical literature of older, as well as more recent times, is rich in observations in this direction. Murchison has brought forward twenty-five cases, chiefly taken from English literature, which number might easily be increased one-half by the addition of the more recent, and particularly the German publications,[2] since Leichtenstern himself speaks of having collected thirty-three cases. The retention of such large stones in the small intestines leads to obstinate constipation, then to vomiting of the ingesta, of bilious and finally of feculent matter, to the most severe pains, and the other symptoms of acute peritonitis. These symptoms continue until death ensues, or until the time when the hitherto impacted stone passes forward into a wider portion of intestine, and the impaction is therefore relieved. Although such cases may end in death, still the expulsion of the stone through the anus, and the almost immediate recovery of the patient, occurs often enough, despite the most severe phenomena of disease, sometimes just at the moment when stercoraceous vomiting has set in. In Osmond's case (London Med. and Surg. Journ., 1836) the fæcal vomiting lasted fully three weeks, and it, nevertheless, resulted in the expulsion of the stone and the recovery of the patient.

Gall-stones which have arrived in the intestinal canal by the natural way, through the ductus choledochus, are, as a matter of course, not in any great danger of becoming impacted in the comparatively wide intestinal canal. As a rule, therefore, it may be presumed that gall-stones which become the cause of closure of the intestines have made a way for themselves by a fistula from the gall-bladder into the intestines (compare the interesting observation of Cohnheim, Virchow's Arch., Vol. 37). This method of entrance is established almost beyond a doubt if it has not been preceded by jaundice, etc. Other cases, however, are so described that we are forced to the conclusion that the stone in question, despite its enormous size, has passed through the

[1] Compare the detailed account of this condition by Leichtenstern in this Cyclopædia, Vol. VII., p. 573.

[2] Compare *Cohnheim* in Virchow's Arch., XXXVII., p. 415. *Dessauer*, ibid., LXVI., p. 271. *Koestlin*, Würtemberg Corr.-Bl., 1876, April 5. *Barker*, The Lancet, 1878, Feb. 23d, p. 278.

ductus choledochus into the duodenum. In view of the apparent or actual disparity that exists, in some of the reports, between the size of the stone and the path by which it is claimed that it reached the intestinal canal, we would remind our readers of what has been stated above regarding the possible growth of stones in the intestinal canal by the deposit of mucus and fæcal masses about them, and that biliary concretions have repeatedly been found enclosed as a nucleus in the centre of large intestinal stones. It is likewise known that uncommonly large gall-stones may remain lying for a long time in pocket-shaped dilatations of the walls of the duodenum or jejunum without causing closure of the intestines, although this may still finally follow as soon as the concretion leaves its previous location to move forward in the intestine.

The impaction of such large gall-stones takes place most readily at the lower end of the ileum, immediately above the ileocæcal valve. But cases have been reported in which the stone has been arrested within the large intestine, especially in the rectum, just above the sphincter ani. Agglomerations of stones, cemented together by fæcal masses, have also been found arrested at this point. Despite the most severe pain and the most obstinate constipation thereby called forth, we usually see these stones at last expelled per anum, whereupon immediate recovery follows.

Finally, gall-stones which have been retained for some time within the intestinal canal may cause *ulceration and gangrene of the intestinal walls*, and thereby lead to *perforation of the intestine*, the stones either escaping into the cavity of the abdomen or being expelled through the abdominal walls. When there is closure of the small intestine by means of large biliary concretions, perforation does not, as a rule, take place. The fatal termination is reached before this can be developed. On the other hand, perforation may be looked for when the stone is situated in a portion of the intestine where it can lie for a considerable length of time without causing intestinal obstruction. Thus, stones which remain in the cæcum in particular may cause ulceration, gangrene, and fatal peritonitis by perforation. It is rare that (smaller) gall-stones pass into the

vermiform appendix of the cæcum, and, as is so often the case with other foreign bodies at this point, cause ulceration and perforation of the vermiform appendix and death by peritonitis.[1] Sirey even describes a case (Med. Times and Gaz., 1859, II., p. 372) in which a circumscribed abscess developed about the vermiform appendix, and a gall-stone enclosed in the latter finally made its escape through an ulcerative opening in the abdominal walls. Jeaffreson saw two large gall-stones in a pocket-shaped dilatation immediately above the ileo-cæcal valve. The spot ulcerated, and perforation with fatal peritonitis followed. At the autopsy, one of the stones was found to have escaped into the abdominal cavity.

Symptomatology.

It is a well-known and undoubted fact that gall-stones of the most varied number, size, and general characteristics may occur *in the gall-bladder*, and remain there a long time without causing the slightest disturbance or betraying their presence by any symptom whatsoever. This course of behavior is looked upon by many physicians as constituting the rule, while others doubt it more or less positively (Fiedler). Perfect indifference of the gall-bladder to stones is observed particularly in persons of advanced age, whose organism shows itself more indolent in every respect than that of younger people. It is true that large and numerous stones lying within the gall-bladder may sometimes cause an indefinite sensation of discomfort, tension, or distention in the region of the gall-bladder. Sensations of this kind are liable to appear more distinctly some time after a meal, or as the result of strong bodily exertion, as well as after jarring of the body in walking over uneven roads, riding or driving. Some patients with gall-stones complain of a feeling like that of a solid body rolling about inside of them when they turn over in bed.

The presence of gall-stones sometimes causes a more or less active irritation of the nerves of the gall-bladder, which may extend to neighboring nerve-areas, and occasionally cause vomiting

[1] Instances of this kind have been observed by *Budd* (Diseases of the Liver, German transl. by Henoch, 1846, p. 325), and by *Trousseau* (Clinique méd., II., p. 536).

or other disturbances of the stomach and bowels. Indeed, the pressure upon the stomach of a gall-bladder filled with stones may even give rise to the symptoms of stenosis of the pylorus. It is easy to understand how, in persons with great sensitiveness of the nervous system, a gall-bladder overloaded with concretions may give rise not only to disagreeable sensations of the most varied kind, but to real conditions of disease, even in distant organs, accompanied with psychical depression and a hypochondriacal mood.

When the gall-bladder is very full of stones, it sometimes constitutes a tumor which can readily be felt through thin abdominal walls, and whose hard and nodular character soon betrays its nature to the physician. In palpating this tumor, in rare cases a peculiar, soft, crackling sound is recognized, about such as would be caused by grasping a handful of hazel-nuts in a bag (J. S. Petit). This sound can be recognized still more distinctly by means of a stethoscope, while at the same time pressure is made upon the tumor.

For the symptoms which accompany inflammation and ulceration of the mucous membrane of the gall-bladder caused by stones, as well as for the signs by which the results of this condition betray themselves, we refer our readers to what has previously been said (compare cholecystitis, p. 550). Such inflammations generally remain latent until the time when they likewise extend to the serous membrane. The fact that an attack of cholecystitis depends on gall-stones is to be deduced more from the history of the case and other circumstances connected with it than from any definite phenomena in the status præsens. The occurrence of severe symptoms connected with the peritoneum is generally the first thing that attracts our attention to this dangerous condition, without our even then recognizing gall-stones as the direct cause. If the cholecystitis leads to shrinking and devastation, to the calcification or ossification of the gall-bladder, this remains perfectly latent, or, at most, is accompanied by indefinite sensations of pain or pressure, which in themselves could not with certainty be referred to gall-stones.

Gall-stones which lie quietly in the hepatic *ducts* and fill them, seldom give rise to such characteristic symptoms that a diagnosis

can be based upon them. Contrary to all expectation, such stones often cause neither jaundice nor swelling of the liver. Smaller concretions in this situation do not even occasion any disagreeable sensations, pain, and the like. In some cases, however, such stones call forth a continuous sensation of weight or dull pain in the region of the liver, which from time to time is suddenly interrupted by colicky attacks of severe, cutting pain originating in the right hypochondrium, and radiating thence toward the breast and the lower abdomen. In other cases stones within the liver-passages call forth well-marked chills, with severe fever and sweat following—attacks which bear all the characteristics of a paroxysm of intermittent fever, and are also sometimes repeated at quite regular intervals.[1] Fauconneau-Dufresne (l. c., p. 195) communicates a case of this kind belonging to Trousseau, which is distinguished by the severity of its symptoms, especially the severity of the pain, as well as the long duration of the complaint. Trousseau here made the diagnosis, based on the paroxysms of pain as described above, as well as on the presence of biliary concretions in the stools.

The sharpest contrast exists between the insignificant symptoms caused by gall-stones during their quiet sojourn in the bladder or the liver-ducts, and the severe manifestations that arise when these stones are set in motion and advance through the excretory ducts toward the intestine. This group of manifestations is known under the designation of

Biliary or Hepatic Colic (Colica Hepatica).

Hepatic colic and the passage of gall-stones through the larger excretory ducts are certainly two things which do not entirely cover the same ground. For, on the one hand, the group of symptoms belonging to hepatic colic may also be induced by means of other foreign bodies occurring in and passing through the biliary passages, for instance, by echinococcus cysts, round-worms, etc. And, on the other hand, it is an old experience which has often been observed by physicians at certain watering-

[1] Compare farther on the description of this so-called *Fièvre intermittente hépatique* according to Charcot.

places (Karlsbad, Vichy, etc.), that numerous smaller concretions may be expelled with the fæces without having been preceded by even the slightest discomfort that might be referred to their passage through the biliary canals. It is therefore probable that attacks of colic only occur when the walls of the canal are greatly distended and torn by the stone. If the canal is narrow and the stone somewhat large, there will not fail to be colic. On the other hand, in the case of more aged and sluggish individuals, such "crises" may take place perfectly unobserved.[1] Indeed, Beau has even gone so far as to assert that hepatic colic is only exceptionally caused by gall-stones advancing through the biliary passages; that, as a rule, it is a pure neuralgia without the interposition of any foreign body. Beau refers, among others, to a statement of Chomel, according to which, in thirty to forty cases of hepatic colic, gall-stones were hardly found once in the stools. This assertion, however, stands in direct antagonism to the experience of those who have given this subject their full attention. Frerichs, Trousseau, Willemin, Murchison, and many others teach that we rarely fail to find stones in the stools after attacks of hepatic colic. In forty-five carefully observed cases of hepatic colic Wolff invariably found the stones in the stools. The examination of the latter, to be sure, must not only be made carefully, but also continued long enough, for cases have been known where the stones did not pass away by the anus until four or five days after the attack of colic. Nor may we follow the advice of Prout, who recommends that the fæces be thrown into a vessel of water, when the stones will float on its surface. This advice is erroneous, because gall-stones in their *moist* condition are never lighter than water. The best plan, therefore, is to cause the fæcal mass (which, according to circumstances, may have been previously mingled and diluted with water) to be strained through coarse gauze, or, better yet, passed through a sieve which is not too coarse.

[1] *Fagge* (Guy's Hosp. Rep., 1875, Vol. XX.) states that a man who died as the result of a hernia had shortly before been attacked with jaundice which was unaccompanied by pain. His gall-bladder contained numerous stones; the ductus choledochus was so wide that it would admit the finger. Evidently gall-stones had here been passed, although without causing any colic pains.

The attack of colic sometimes appears in the midst of the most perfect good health; at other times it is preceded by certain *prodromata*. These consist of a sensation of nausea and considerable distention of the abdomen, of unusual nervous excitement and increased sensitiveness, of frequent yawning and shivering. The attack itself generally begins two or three hours after the principal meal, if it is not caused by great muscular exertion or by jarring the body. In the majority of patients the *pain* of colic begins moderately, and increases gradually, though pretty rapidly, in severity. In many cases, however, the patient is suddenly and quite unexpectedly attacked with the most severe pain. It begins at the epigastrium and radiates toward both hypochondriac regions, the spine, the shoulders, especially the lower angle of the right shoulder-blade (Wolff), or toward the neck, or even the right arm. According to Trousseau, the pain is also said to descend into the abdomen, and thus sometimes to acquire a certain resemblance to renal colic, a statement which Murchison, with all his experience, is not able to confirm.

With regard to the degree and character of colic pain, it will be found that a dull, continuous sense of pain is constantly present during the entire duration of the attack, but from time to time this undergoes a paroxysmal increase up to the most fearful height. This acute pain, which comes and goes in paroxysms, is described by the patients as a boring, tearing, burning, or constricting sensation. The paroxysms are so extreme and torturing that the patient doubles himself up, draws up his knees, and rests his chin on them, but also constantly changes his position, hoping in some way to obtain relief. Women who have borne children declare that the pains of labor are nothing compared to those of hepatic colic.

In persons of a nervous constitution the pain sometimes causes fainting, delirium, or even epileptiform *convulsions*. In hysterical women the irritation of gall-stones not only sometimes causes an hysterical seizure, but the symptoms of hepatic colic may also be associated with those of hysteria (Bamberger).

If the paroxysmal exacerbations of pain are often repeated and of long duration, they leave behind them great lassitude and exhaustion, the patient's face grows pale, the pulse weak, and

the entire body is bedewed with cold sweat. In some rare cases profound collapse sets in, which has occasionally been seen to end in death.[1]

The abdomen usually presents no deviations during the attack from its ordinary condition. Occasionally it is hard and resisting, on account of the tension of the recti muscles, or it may be distended from meteorism. During the first part of an attack of colic the pain may be somewhat relieved by pressure from without. But after it has continued for some time there is great sensitiveness in the region of the gall-bladder, or even a well-pronounced sense of pain, which also continues for some time after the seizure. In some instances a swelling of the liver has also been recognized during the attack (Beau, Wolff). The local pain in the region of the gall-bladder may become very severe if a greater degree of inflammation of this organ exists.[2]

In severe and long-continued attacks of hepatic colic it is not uncommon to have sensations of chilliness or even the most severe chills occur in the midst of the pain. These recur sometimes at variable periods, sometimes quite periodically, with the regularity of an intermittent fever. It is thought that these chills depend on the excessive stretching and tearing of the biliary passages. They are evidently, like the rigors in catheterization of the urethra, due to the fact that the excitation of the sensitive nerves of the liver is carried in a reflex manner to the vaso-motor centre, and through the agency of the latter causes spasm of the small cutaneous arteries, ischæmia, etc.

The attack of colic is, as a rule, accompanied by *vomiting*, which is repeated several times, and may become very severe. The patient first expels all the food contained in his stomach. If the vomiting is long continued, and the ductus choledochus is completely obstructed, the only thing brought up is sometimes large quantities of a colorless and acid fluid. If considerable

[1] *Murchison* has several times seen an attack of hepatic colic end in coma and death in persons whose urine was albuminous. It appears, therefore, that under the influence of an attack of colic an acute uræmic condition may be developed.

[2] *Trousseau* has called attention to the fact that occasionally a severe attack of hepatic colic is followed by intercostal neuralgia, the existence of which is betrayed by the circumstance that pressure over several of the spinous processes causes acute pain.

quantities of bilious matter are vomited, it is an evidence that the bile-duct has again become pervious. The act of vomiting is usually followed by temporary relief of pain. Very often it is accompanied, especially in nervous individuals, by distressing hiccough.

As a rule, the bowels do not move during a paroxysm. Exceptionally there is diarrhœa, or constipation alternating with diarrhœa (Wolff).

After these symptoms have lasted from twelve to twenty-four hours, *jaundice* generally appears, the conjunctiva usually first showing a yellow hue, which rapidly spreads over the skin of the entire body. The jaundice is more or less pronounced, according as the closure of the bile-duct by the stone is complete or not, and according as the closure lasts for a longer or shorter time. The urine,[1] in well-marked icteric discoloration of the skin, contains biliary constituents, and thereby receives a dark mahogany-brown color, while the fæces are correspondingly paler, often entirely discolored.

The appearance of jaundice settles the nature of the attack as being one of hepatic colic, the jaundice itself being due to closure of the ductus choledochus. But this symptom is by no means always present.[2] For if the stone makes its way into the intestine after having been arrested within the common duct less than from twelve to twenty hours, or if it does not advance beyond the cystic duct, or if it is of angular form and the bile can flow alongside of it, no jaundice will occur, although hepatic colic is present. By bearing this in mind, we shall understand those cases in which people suffer repeatedly from attacks of colic, which are regarded as gastric colic because no jaundice ever appears, and in which the subsequent course of the disease leaves no doubt that the paroxysms of pain were really due to

[1] At the beginning of a seizure, before the occurrence of jaundice, the patient often passes large quantities of pale watery urine (the so-called urina spastica or nervosa). Exceptionally, under quite peculiar influences, just the same sort of urine is also evacuated during the continuance of the jaundice, although the urine which is passed shortly before and after may be rich in biliary constituents (*Murchison*).

[2] A striking statement is made by *Wolff* (l. c.) to the effect that in forty-five cases of well-marked hepatic colic, in which gall-stones were found in the fæces, jaundice was absent twenty-five times.

the presence of gall-stones. In such cases the diagnosis is sometimes confirmed by observing that the attack of pain is associated with a very slight yellow coloring of the conjunctivæ at least, or that the urine shows small quantities of biliary coloring matter.

The duration of the jaundice varies according to the number and size of the stones, but it generally does not last longer than a couple of days—at most, a couple of weeks. Permanent closure of the ductus choledochus and chronic jaundice caused by gall-stones is, on the whole, of rare occurrence, since stones which have passed the cystic duct can generally find their way through the extremity of the common duct. At the same time, examples are not wanting in which gall-stones have been impacted in the ductus choledochus, causing chronic icterus that has continued until death. The jaundice caused by gall-stones has this peculiarity, that it may return at various intervals, whether it be that all the stones do not leave the gall-bladder at the first attack, or that new ones have been developed in the meantime. We must also remember, that when a somewhat larger stone has once passed the ductus choledochus, this canal may remain permanently dilated, so that subsequent smaller stones neither cause jaundice nor colic.

So far as *temperature* and *pulse* are concerned, hepatic colic is, as a rule, not accompanied by fever, the temperature of the body is not raised, and the frequency of the pulse is more likely to be below than above the normal. Wolff even remarks that, in uncomplicated cases of hepatic colic, the frequency of the pulse will be found from five to ten beats less than at a time when there is no paroxysm; and he thinks that in doubtful cases, where there is no jaundice, etc., this symptom might constitute one of the main grounds of the diagnosis. And, indeed, the diminished frequency of the pulse is observed as well when jaundice is present as when it is absent; this symptom, therefore, cannot be regarded as belonging to the jaundice, that is, to the influence of the biliary acids upon the innervation of the heart. Other observers, on the contrary, state that the pulse is moderately frequent during the continuance of colic, and that in severe paroxysms it may become small and even imperceptible.

A temporary rise of temperature is said not to be infrequent just at the time when the patient is chilly and his extremities feel cool to the touch. If inflammation and ulceration of the biliary passages is caused by the stones, then continuous or intermittent fever may exist even after the paroxysm of pain itself has passed. Under such circumstances new seizures are often accompanied with fever and subsequent sweats.

When the attack of colic ceases, slight perspiration generally sets in, by means of which the patient feels much relieved. If the attack is severe, the patient is fairly bathed in perspiration. As soon as the pain has subsided, the urine generally throws down an abundant sediment consisting of urates.

If the closure of the bile-duct continues for some days we may often remark a uniform *swelling of the liver*, and discover a pear-shaped tumor, sensitive to the slightest touch, corresponding to the position of the gall-bladder,—manifestations which may be explained by the dilatation of the biliary passages from pent-up bile.

Mere *biliary gravel*, without the presence of actual gall-stones, seems likewise capable of calling forth attacks of genuine hepatic colic. Frerichs speaks of a case of this kind, in which, after the attack of pain, a large number of little blackish-brown granules were seen in the stools, such as are liable to be precipitated from thick, stagnating bile. There were no actual stones found with them. The brown granules appeared for six days, and the patient then seemed to recover. As a rule, the passage of biliary gravel appears to go on in a perfectly latent manner, excepting those cases where there is such an amount of gravel that its escape from the anus is accompanied by severe pain (Chauffard).

The duration of the paroxysms is very variable; as a rule, the actual colicky pain lasts several hours, but in some cases it may continue several days. If it lasts long, however, the pain makes longer or shorter pauses, showing distinct remissions, though never being entirely lost. The close of the attack is seldom sudden, more frequently it is gradual, with the diminution of the symptoms described, and especially of the pain. If the stools which are passed after the attack are examined—and they should

be carefully inspected after every such paroxysm—they will usually be found to contain the biliary concretions which have given rise to the affection, sometimes in a well-preserved and sometimes in a crumbled condition. The number of the stones varies very greatly—there being sometimes only one, sometimes several, a few or a large number especially of smaller stones. (Pujol once counted more than a hundred of them.[1]) As was remarked above, the examination of the fæces for biliary concretions must extend over several days, as the stones are sometimes not evacuated until after four or five days. If, despite careful examination during the time mentioned, no gall-stones appear in the stools, it is possible, in cases where there is no jaundice, that the stones which had entered the cystic duct have returned into the bladder.

Although severe seizures are associated with the most fearful suffering to the patient, and the symptoms often assume a most threatening character, still experience teaches that we may, in general, feel easy with regard to the result. Even the most violent paroxysms of hepatic colic are liable to terminate favorably, and after the cessation of the pain the patient feels extremely relieved, as if new-born, although a certain degree of weariness may remain for a while, according to the individuality of the subject. It is only in very exceptional instances that severe attacks of colic have terminated in collapse and death. Portal, Bogras, Cruveilhier, and others have witnessed such cases, where at the autopsy no other cause of death could be found than the gall-stone enclosed in the biliary passage.

Attacks of greater or less severity, such as have been described, are then repeated more or less frequently at irregular intervals, so that some patients have to endure more than forty or fifty. This state of things is explained by the fact that the stones contained in the gall-bladder are not all evacuated at once, but that they enter the biliary passages in successive groups. Perhaps, in some patients, the development of new gall-stones may have taken place in the meantime. The repeated

[1] The massive size which concretions may attain appears from an observation of *Bermond* (Lancette française, 27 Févr., 1834), who found an agglomeration of faceted stones as large as two fists.

paroxysms generally arise spontaneously—that is, without any known exciting cause. Sometimes they are referred by the patients to great emotional disturbances—an outbreak of anger or the like—or to unwise indulgence in eating, to indigestion, and other similar circumstances. Whereas, in one patient several months or even years elapse between the attacks; in another, they will follow one another with extraordinary frequency. Occasionally, there is even a certain sort of periodicity to be noticed in this matter, inasmuch as the paroxysms always occur at certain definite seasons of the year. Although the time which intervenes between the first and the last seizure is subject to the greatest variation, still, on an average, it may be admitted that in most patients (and in pure uncomplicated forms of hepatic colic) the entire series is liable to be comprised within a period of from two to twelve months (Wolff).

During the period that intervenes between two attacks the patient often finds himself perfectly well, though generally certain signs still indicate that the trouble is not at an end. The conjunctiva then shows a slight yellowish tinge which, at times, grows more prominent; the digestion and action of the bowels are irregular and disturbed in various ways; the psychical condition is often depressed or very irritable. The swollen liver is sensitive to pressure, or even the seat of a spontaneous, dull sensation of pain, the gall-bladder may be felt as a fluctuating tumor, or as a hard, round lump. In very rare cases we may directly recognize the stones in the gall-bladder by the sense of touch.

The symptoms which are evoked by gall-stones that are long arrested in their progress through the biliary passages, perhaps even permanently retained within the same, or which leave the gall-bladder by unnatural ways, vary to an extraordinary degree, according to the peculiar circumstances of the case.

Gall-stones which are impacted in the neck of the gall-bladder, or in the ductus cysticus, at first call forth the usual symptoms of hepatic colic, with the absence of jaundice. If the stone,

then, contrary to the usual rule, again falls back into the neck of the bladder, the attack of colic therewith ceases, of course without permitting the concretion to be discovered in the passages from the bowels. It has been found, as an accidental post-mortem discovery, that the neck of the gall-bladder is occasionally occupied by a gall-stone wedged into it, without any symptom, during life, having excited the suspicion of such a state of things. The same thing is true of gall-stones which remain lying quietly in the cystic duct (generally permanently). Although they are here closely surrounded by the walls of the canal, still we cannot exactly speak of the impaction of these stones, because we have accustomed ourselves to associate with this word the idea of some severe symptoms. If no tumultuous contractions of the gall-bladder take place, which would force the stone forward, and thus tear or stretch the walls of the biliary canal, the stone remains unmoved in the cystic duct, without betraying itself by any direct symptom. The occurrence of dropsy of the gall-bladder is the first thing that arouses the suspicion of a closure of the cystic duct, the cause of which will not be attributed to an impacted stone unless the patient has, at some former time, given evidences of cholelithiasis, and particularly of hepatic colic.

Gall-stones which are accidentally held fast in the *trunk of the hepatic duct* (which, in view of the anatomical relations of the same, must certainly happen but very rarely), if they completely close the passage, must necessarily give rise to icterus, swelling of the liver, and, in case of considerable tearing or stretching of the walls of the canal, also to hepatic colic, with vomiting, etc.; in short, to all the symptoms of closure of the common duct, except that there will be no enlargement of the gall-bladder unless the common duct is also at the same time closed.

The symptoms of stones in the ductus choledochus differ according to the varying relations in which the stone stands to the orifice of the canal. The severe colicky pains which accompany the passage of a stone through the cystic duct are usually somewhat lessened when it reaches the common duct, on account of the greater width of the latter. But, at the same time, jaundice is now likely to appear. As soon, however, as the stone arrives in

front of the diverticulum, and undertakes to force itself through, the pains return with increased violence. With its passage through the diverticulum the pain sometimes ceases suddenly, as if by a stroke of magic. If, on the contrary, the stone remains impacted fast in the common duct, it calls forth, above all things, permanent jaundice, often continuing until death. The other symptoms, especially the pains, depend greatly upon the form of the stone and the character of its surface perhaps even more than upon its size. A rough or angular stone causes more pain than one which may be larger, but is at the same time round and smooth. On the other hand, irregularly shaped, angular stones are more likely to permit of some bile flowing past them, and this will have an influence on the intensity of the icterus. The latter, indeed, hardly shows traces of its presence in some cases of this kind.

The futile efforts made by nature to force the stone through the diverticulum, as well as the final successful attempts at its expulsion, make themselves known by the usual manifestations of hepatic colic. But if, despite this, the stone will not advance, the tempestuous attacks of colic gradually subside, first making longer pauses, and then ceasing entirely, after having lasted for a longer or shorter period, sometimes eight to fourteen days. The stone remaining in the ductus choledochus, if it is firmly enough grasped by its walls, now causes only the symptoms of closure of the common duct, as we have described them above (p. 603), viz., chronic icterus, dilatation of the biliary passages, sometimes also suppurative cholangitis, swelling of the liver, etc. If, on the contrary, the stone is but loosely grasped by the walls of the duct, so that the bile can flow down past it, all symptoms may be entirely wanting for a considerable time. Reference must still be made to an important manifestation, to which stones that are permanently enclosed in the common duct or in the hepatic duct give rise, whether they are firmly impacted, or lie loose and movable within the canal. This is, namely, a peculiar (symptomatic) form of *intermittent fever*.

This must not be confounded with the fever which is one of the manifestations of hepatic colic, for it does not arise until a time when the latter is past. Indeed, the intermittent fever in

question, to which Charcot has given the designation of *fièvre intermittente hépatique*, does not only arise on the closure of the excretory ducts in question, through gall-stones, but it may show itself whenever there is a long-continued or permanent closure of the ductus choledochus from any cause whatsoever.

According to Charcot,[1] the anatomical conditions which might be regarded as favorable to the production of this form of intermittent fever are the presence of pus or muco-pus, mingled with stagnated bile, in the dilated biliary passages. At the same time it is certain that purulent cholangitis occurs without fever, as well as, on the other hand, that the latter may occur without any pus in the ducts. Nor is it necessary that there should be abscesses in the liver in this kind of fever. Charcot, therefore, seeks to explain these attacks of fever upon the following hypothesis: That intermittent hepatic fever depends on a *septic principle* present in the dilated and inflamed biliary passages, a pyrogenic material which arises from the alteration or decomposition of bile. The nature of this principle itself is as little known as is the immediate cause of its development.

Charcot describes the signs of *intermittent hepatic fever* as follows, based on twenty observations by himself and others:

Jaundice may be present or not. It is often not present; for instance, in biliary gravel or in stones within the liver-ducts, which latter are especially liable to give rise to this symptomatic intermittent fever.

Hepatic colic may introduce a series of febrile attacks, or may precede them by some time, or, indeed, may not be present at any time (for instance, in stones of the liver-ducts).

The *febrile movement* itself appears suddenly, begins with a severe chill, and all its stages proceed as in genuine idiopathic intermittent fever. The chill is sometimes very severe, the patient is shaken about vigorously in his bed, his temperature rises to 102.2°, 104°, or even 105.8° Fahr. The subsequent sweat is sometimes very abundant. In some of the cases under consideration, however, one or another stage of the attack was absent, and this was especially liable to be true of the sweating stage.

[1] Leçons sur les maladies du foie et des reins, publiées par Bourneville et Sevestre, Paris, 1877 (p. 178 et seq.).

The *non-febrile intervals* are often sharply defined, the apyrexia being complete. The recurrence of the fever usually follows with the same regularity as in a legitimate quotidian, tertian, or quartan. At the same time, there certainly are many exceptions to this rule.

A remarkable peculiarity of these attacks of fever, which, however, has thus far been only once proven (Reynard[1]), seems to be the *diminution of the excretion of urea* during the attack, while idiopathic intermittent paroxysms, as is well known, are associated with increased excretion of urea. After the attack, the urine also contains leucin and tyrosin. Charcot explains the symptom concerning the amount of urea, on the assumption of an insufficient function of the parenchyma of the liver during the fever.

As is generally the rule in symptomatic fevers, so also in this form the rise of temperature generally sets in about evening, whereas idiopathic intermittent attacks usually occur in the morning.

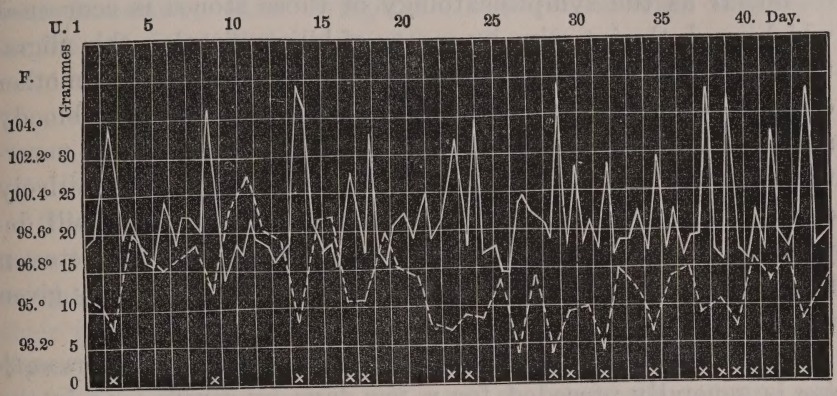
Intermittent hepatic fever is generally in so far chronic that it may extend over a period of two or three months, although with intervals of freedom from fever of eight, ten, or fifteen days. As many as thirty-one attacks of this kind have been counted in a patient (Reynard).

The accompanying curve shows the course of the body temperature and excretion of urea in the patient observed by Reynard (abbreviated from the original in Charcot's "Leçons sur les maladies du foie et des reins"). The continuous line represents the temperature, the interrupted line the urea. The asterisks at the foot of the diagram mark the days during which a paroxysm of hepatic intermittent fever occurred.

This fever may have a *favorable termination*, as appears from a case of Henoch. After repeated attacks of colic intense jaundice developed, with which intermittent fever soon became associated, which was supposed to be due to a hepatic abscess, and was dissipated by quinine. The patient was sent to Carlsbad, and here she had renewed paroxysms of colic. The stools, however,

[1] Gazette médic. de Paris, 1873, No. 49.

were again colored with bile, and fourteen faceted gall-stones were evacuated from the bowels, whereupon a cure followed. But a *fatal termination* is decidedly the rule. Death follows sometimes in the midst of severe manifestations which remind



U = urea excreted.

one of pernicious swamp-fever, sometimes in the course of a remittent fever with typhoid symptoms, which has taken the place of the symptomatic intermittent.

When stones which have been arrested in their progress through the biliary passages give rise to *laceration of the duct*, or when they cause inflammation and ulceration of the biliary passages, terminating in *perforation* of the same, then the clinical history, which at first had all the characteristics of ordinary biliary colic, is suddenly transformed into one of an extremely threatening character. For now we have the symptoms of perforation and rupture—that is, of acute perforative peritonitis—which is likely to terminate in rapid death.

With reference to the symptoms to which stones lying within the liver-ducts give rise if they cause inflammation and ulceration, which, according to circumstances, extend to the tissue of the liver and to the branches of the portal vein, we refer our readers to the symptomatology of cholangitis, of suppurative hepatitis, and of pylephlebitis.

During their sojourn in and their progress through the *intestinal canal*, gall-stones, as a rule, call forth no symptoms whatever, especially the smaller ones which have escaped from the bil-

iary passages during the attacks of hepatic colic. It is only quite exceptionally that somewhat larger stones, even if they are not impacted within the intestine, cause more or less severe colicky pains in the bowels, and vomiting as well as great prostration.

So far as the symptomatology of those stones is concerned which reach the intestine by means of biliary fistulas, this migration sometimes takes place in a perfectly latent manner; in other cases, however, severe pains in the bowels, vomiting, bloody stools, and other symptoms have been observed, which, nevertheless, are not sufficient to establish the diagnosis positively during life. The severity of the symptoms concerned will depend essentially on the relations of space which exist between the size of the stone and the width of the fistula in any given case.

The expulsion of gall-stones *through the stomach by vomiting* is generally preceded for a few days by severe pain in the stomach, combined with persistent and powerful efforts at vomiting.

Gall-stones that are *firmly impacted in the intestinal canal* first of all cause obstinate constipation, with which there are associated colicky pains, of continually increasing severity, at a part of the abdomen corresponding to the seat of the impaction. If the closure of the intestine is complete, vomiting occurs, first of the ingesta, then of masses abundantly colored with bile, and, finally, there is stercoraceous vomiting. At the same time the abdomen is distended and tense, the patient is almost incessantly tormented with the most severe pain, his countenance is altered—in short, the symptoms of intestinal obstruction, or of the peritonitis of obstruction arise. These symptoms sometimes show a certain abatement, which may depend on the fact that the stone advances slowly, and thus sometimes lies in narrower, sometimes in wider portions of the intestine. All the symptoms cease with the final expulsion of the stone, or they continue, the condition progressively growing worse, until the death of the patient. Inasmuch as stones of a size large enough to cause obstruction of the bowels, as a rule, reach the intestinal canal by way of a fistula, the symptoms of obstruction are usually not preceded by attacks of hepatic colic, nor by jaundice, unless

there happens to be a complication with catarrhal jaundice or the like.

Finally, stones which are retained above the sphincter ani cause obstinate retention of stools and severe pains, sometimes with tenesmus; these symptoms, however, at once disappear on the expulsion of the stone.

Diagnosis.

The requirements of diagnosis are not restricted to a determination of the existence of cholelithiasis, but it must also decide to what symptoms the calculi give rise when quietly resting at their place of development, and to what consequences they lead when they change their position in any direction.

In a goodly proportion of cases, cholelithiasis remains unnoticed, because the gall-stones do not give rise to any symptoms. They are especially overlooked in old people, in whom the sensibility of the visceral nerves is considerably obtunded, or when, in addition to the cholelithiasis, other abnormal processes are present by which the symptoms of the former are concealed.

As a rule, the gall-stones which are situated in the gall-bladder escape diagnosis; for, although from the subsequent symptoms of hepatic colic, etc., we may surmise that calculi are present in the organ, there can be no question of a diagnosis, in the true sense of the term, except in those extremely rare cases in which we are able to feel the gall-bladder as a hard, nodular tumor through the abdominal walls, or in which a slight creaking or crackling reveals the presence of the concretions in the organ. All other subjective and functional symptoms which may be relied upon for diagnosis are more or less uncertain and deceptive.

The same statements will hold good with regard to the demonstration of calculi in the hepatic ducts. It must be left to the judgment and powers of combination of the physician to draw a probable conclusion from the circumstances of the individual case with regard to the presence of stones in the hepatic bile-ducts, but the autopsy alone will furnish positive results.

With regard to cholecystitis and cholangitis calculosa and their sequences, we refer to the previous remarks. In these conditions, also, the attempt at diagnosis rarely leads to more than a conjecture, except in those cases in which perforation and rupture clear up the existing obscurity.

The diagnosis of cholelithiasis is generally based on an attack of so-called gall-stone colic. We know, however, that the passage of calculi through the bile-ducts may also occur latently. J. Frank had remarked that small calculi often pass unexpectedly in the stools, although this had not been preceded by the slightest symptoms; even somewhat larger concretions may escape without symptoms. In most cases of this kind it is probable that the bile-ducts had been previously dilated. It is a noteworthy fact, to which attention has been called by the physicians of certain watering-places, that previously latent cholelithiasis becomes unmasked under the use of alkaline mineral-waters, and evidently because, in consequence of the increased secretion of bile, the previously stationary calculi undergo active motion, and are forced into the excretory ducts by the stream of fluid.

All observers are of the opinion that paroxysms of hepatic colic, when fully developed, cannot be mistaken for any other affection. But difficulties may, however, arise, especially when the physician has to deal with the first manifestations of cholelithiasis—the first attack of hepatic colic. Caution demands, under such circumstances, that a positive diagnosis should not be made until the calculi have been actually found in the passages. The more frequently the paroxysms occur, the easier it is to determine their true nature. The mere fact that a patient has been several times affected with jaundice, especially when this develops shortly after a paroxysm of pain starting from the region of the liver, indicates almost positively that these symptoms are due to gall-stones.

The most important indications that an attack of colic should be regarded as hepatic colic, and that gall-stones are passing through the bile-ducts, consist in the character and situation of the pain, in the concomitant disorders of the digestive apparatus (nausea, vomiting), in the condition of the abdomen, in the supervention of icterus and the time of its appearance, in the condition

of the pulse (which presents at least no considerable increase in rapidity, however variable it may be in other respects), in the absence of any elevation of temperature, and finally in the presence of calculi in the stools. Although one or the other of these symptoms is occasionally absent, the ensemble of the others is a sufficient basis for diagnosis. Icterus *per se* possesses no great diagnostic importance, as it may be present in many other conditions and be absent in hepatic colic. When present,[1] however, it is of great assistance in diagnosis, and also furnishes indications with regard to the situation of the moving gall-stones.

In cases in which jaundice is absent, it may be readily mistaken for cardialgia, especially during first attacks. The diagnosis of gall-stones as the cause of the paroxysm is favored when the region of the gall-bladder is sensitive on pressure, and when this organ can be felt as a rounded tumor, as usually occurs under such circumstances. In gastric neuralgia the pain is situated more in the pit of the stomach; in hepatic colic, more in the right hypochondrium. In the former the pain usually appears immediately after the ingestion of food, while in the latter it only develops a few hours after meals. In hepatic colic, also, the digestive organs are usually affected in a different manner than in cardialgia. The examination of the fæces for gall-stones will almost always remove any doubts which may still be present.

The spasmodic and colic-like affections of the abdominal organs (intestinal and renal colic), external and internal strangulation of the gut, lead colic, inflammation of the peritoneum, and various abdominal viscera may also, at the onset, be mistaken for hepatic colic, though not as readily as cardialgia. But a careful examination of the patient, and a full previous history, will, in such cases, furnish so many differential data that it is hardly conceivable that these conditions should, for any length of time, be mistaken for hepatic colic.

Gall-stones are undoubtedly by far the most frequent cause of so-called hepatic colic; but they are not the only cause, as a pure

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[1] According to Durand-Fardel, biliary coloring matters appear in the urine in every attack of hepatic colic, although no distinct yellow color of the skin may be noticeable.

neuralgia of the hepatic plexus also appears to occur, which manifests itself by pains exactly similar to those of gall-stone colic, although not due to calculi. The assumption of true neuralgia of the hepatic plexus is rendered very probable by its analogy to the various visceral neuralgias, which also develop without any demonstrable anatomical lesion of the parts. The problem, however, consists in demonstrating its existence by undeniable facts. This is, however, extremely difficult, as the circumstances of the case are usually such that it also admits of another explanation than that of an hepatic neuralgia. It would be especially injudicious to diagnose true neuralgia when, despite every effort, a calculus could not be discovered in the stools. It only remains for us to mention that men like Budd, Frerichs, and others are convinced that neuralgia of the hepatic nerves occurs independently of gall-stones. "There are forms of neuralgia of the liver," says Frerichs, "which differ materially from colica calculosa in their development, their mode of appearance at monthly intervals, their alternation with other nervous affections, and in their entire course," and he strengthens these remarks by a very remarkable and conclusive illustration from his own experience. Fauconneau-Dufresne regards true neuralgia of the hepatic plexus as a condition which occurs especially in individuals who are predisposed to various neuropathies, and in young chlorotic females. Henoch thinks the disorder is connected with gout and rheumatism, and Beau attributes it to acrid ingesta (which view is combated by the very rarity of this neuralgia). Durand-Fardel, who observed hundreds of patients suffering from gall-stone colic, states that attacks of colica calculosa differ in no respect from those of neuralgia hepatica non calculosa, and that the latter may be accompanied by a very slight and temporary icterus of the integument and urine. The differential diagnosis of the two conditions will, therefore, depend rather upon the circumstances attending the individual case and upon the entire course of the symptoms than upon the peculiarities of the paroxysm.

In very aged individuals cholelithiasis, and even the passage of gall-stones, are often overlooked, because the old do not observe themselves closely and are more indifferent to their bodily

sensations. Such individuals complain, at the most, concerning "spasm of the stomach," by which they are affected three or four times a year, and also concerning a feeling of anxiety, nausea, and vomiting—symptoms which disappear in four to six hours, after which the condition becomes normal until it is repeated after a longer or shorter period. If we observe more closely, however, we will rarely miss a slight icteric color of the conjunctivæ, and the examination of the stools removes all doubt that these disturbances must be interpreted as attacks of gall-stone colic (Trousseau).

According to Durand-Fardel the following factors must be taken into consideration in differentiating simple gall-stone colic from that combined with inflammation of the bile-ducts. When the hepatic region, in the interval between two attacks, is the seat of constant pains, a feeling of tension and annoying fulness, when this continues during the attack, and severe and widespread pains develop on pressure—the inflammatory form of gall-stone colic is present and treatment must be directed accordingly. On the other hand, when the region of the liver appears free in the intervals, or, at the most, a localized pain develops upon pressure on the gall-bladder, when the left hypochondrium is not abnormally sensitive to pressure, and the patient, perhaps, even feels relief from the manipulation—we have to deal with the pure spasmodic form. We must add that the observation of pulse and temperature will readily remove any remaining doubts.

The situation of the calculi may be determined in many cases. When, in the course of an attack of colic, marked jaundice, a fluctuating tumor of the gall-bladder, colorless stools, the absence of bile in the vomited matters, and a dark brown color of the urine are observed, these symptoms indicate that the calculus is situated in the ductus choledochus. Absence of yellow color of the integument, normal color of the urine, and biliary constitution of the vomited matters permit us to surmise, under such circumstances, that the stone is lodged in the cystic duct. But such a conclusion is far from being correct in all cases; the bile may flow past a calculus in the ductus choledochus and the icterus therefore be absent, and, in case the stone is situated

in the cystic duct, it may produce closure of the ductus choledochus by catarrhal swelling of the mucous membrane or in other ways, and thus give rise to jaundice. Calculi in the hepatic duct produce, in general, the same symptoms as those in the ductus choledochus, except that the large, fluctuating gall-bladder is said to be absent in the former. However, it is sometimes absent when the ductus choledochus is closed, or, at least, it escapes our observation. We are completely baffled in those cases in which calculi are scattered throughout several or all portions of the system of bile-ducts.

We have previously indicated how little accessible internal biliary fistulæ are, in the majority of cases, to diagnosis. The considerable size of the gall-stones which pass through the intestines or remain lodged in them, with entire absence of correspondingly severe attacks of colic, may form the basis for the conjecture that the calculi in question have passed through fistulæ into the intestines. While the patient is alive an opinion with regard to the situation of the fistula can very rarely be entertained.

That the symptoms of intestinal occlusion and of internal strangulation in a given case are produced by large gall-stones, may be surmised, with a certain amount of probability, when we have to deal with females at an advanced age; when it appears from the history that an inflammation is or has been present in the right hypochondrium; when the pain is very severe, the vomiting occurs incessantly and with great violence; when the pains are intermittent and develop in numerous paroxysms (because the slowly advancing calculus is now grasped more, now less, firmly by the walls of the intestines), and, finally, from the suddenness with which the last attack of pain terminates in death (Murchison).

Course, Terminations, Prognosis.

Cholelithiasis is, under all circumstances, a chronic disease, whether we include the period of latency or only that of its various manifestations. As we have seen, the attacks of colic continue, in the majority of patients, for a number of months; often, also, relapses occur after intervals lasting years, during

which the patient appears to be entirely free from gall-stones. It is very rarely observed that the symptoms of cholelithiasis cease after a single attack. The entire duration of the disease, whether it manifests itself periodically by paroxysms of colic or remains latent, not infrequently includes several decennial periods, and the individual often carries the gall-stones into the grave.

The usual termination of cholelithiasis, whenever it gives rise to disorders of any moment, is recovery by expulsion of the stones in one way or another, or, perhaps, sometimes by a solution of the calculi within the gall-bladder, etc. This fortunate termination may even then be hoped for, although the disease for a time produces the most distressing suffering. As a rule, the recovery is complete: all the calculi are expelled, no new ones are formed, and the bile-ducts present no indications that they had formerly been in contact with gall-stones. In other cases such traces (cicatrices of ulcers, etc.) remain, but lead to no bad results. Exceptionally the eliminated stones leave the bile-ducts in a condition of ulceration, inflammation, etc., which afterward give rise to obsolescence of the gall-bladder, obliteration of the cystic duct, dropsy of the gall-bladder, or, perhaps, permanent and irreparable occlusion of the ductus choledochus. The last-mentioned disastrous result, like closure of the duct by impacted gall-stones, leads to a condition of marasmus from the chronic icterus, to which the patient usually succumbs within a year.

It may happen that, after the discharge of all the calculi present, the cholelithiasis recovers, but a relapse occurs once or even several times from a continuance of the predisposition to the formation of the calculi.

This cannot, however, be positively determined, since when the symptoms of cholelithiasis appear anew after a certain lapse of time, we cannot state with certainty that no calculus had in the meanwhile been present in the gall-bladder.

We have seen how rarely cholelithiasis terminates in death during a severe paroxysm. It more frequently causes a fatal termination, from the fact that the calculi give rise to perforation or rupture of the gall-bladder or the ducts, to peritonitis, a severe diffuse cholecystitis, with hectic or pyæmic fever, a purulent

hepatitis or pylephlebitis, etc., or that they are impacted in the intestines, and cause ileus, perforation of the intestines, etc. In short, the sufferer from gall-stones is subject to manifold dangers. The untoward course pursued by many cases of this kind is so much more striking, as the transition from entire subjective good health to profound collapse and death often occurs without any warning. As there is no security in any case against such accidents, prudence demands that the physician should give a reserved prognosis, although the latter, as a rule, is good in cholelithiasis. In addition, the prognosis must take into consideration that the disease readily returns after it has remained quiescent for a number of years. On the other hand, it is satisfactory to know that even very protracted and severe cases may finally terminate in recovery, and that we must not prematurely abandon hope with regard to the effect of our therapeutic measures.

Treatment.

The province of the physician consists, in the first place, in the removal of the manifestations of cholelithiasis, especially in combating the attacks of colic, the inflammation of the bile-ducts, etc.; and, in the second place, in the attempt to dissolve the concretions which may have remained, and to prevent the formation of fresh calculi in the biliary passages.

The treatment of the attacks of colic almost always occupies the foreground. We must endeavor to moderate the pains and render the stone movable. This purpose is effected, above all, by narcotics, which are therefore used very extensively, and which, under certain circumstances, must be employed very boldly, as they have, indeed, proven a sovereign remedy in these conditions.

Opium and morphine are the narcotics which are most frequently administered. Although we must, as a rule, endeavor to succeed with moderate doses, it is not advisable to go too far in this attempt, lest we fail in our main object. We may safely resort to full doses, and repeat them, if necessary, as most patients tolerate narcotics very well in hepatic colic, and, even under extraordinarily large doses, symptoms of poisoning do not occur as

readily as in many other conditions. On an average, we may administer 0.05 gramme of pure opium, or 0.015 gramme of morphine, every two hours, until the pain is relieved. The use of subcutaneous injections (0.01–0.02 gramme of morphine) is more advisable than the internal administration, both in order to secure a more rapid action, and also to obviate its rejection by vomiting. The injection may also be repeated from time to time, according to the effects which are observed. The integument of the arm is best employed as the site of injections, as those in the region of the liver present no advantage, and more readily lead to annoyance. In protracted vomiting the opiate may be given in the form of enemata or suppositories.

Among other narcotics belladonna is chiefly employed, and, as is well known, often produces great relief. It is especially serviceable whenever, for any reason, morphine is contraindicated. It has also been recommended for milder cases which run a more chronic course. When given in sufficiently large doses this remedy may be dangerous, as symptoms of poisoning develop quite frequently. As smaller doses are often useless, many physicians restrict the employment of this drug to inunctions of the painful region with belladonna ointment; or 0.03 gramme of extract belladonnæ is given internally every two hours, or suppositories of 0.03 morphine, and 0.06 extract belladonnæ, or subcutaneous injections of 0.004 atropine, and 0.015 morphine every two hours until the pains subside. A liniment of belladonna and chloroform, which is applied to the hepatic region as a fomentation, and is covered with oiled paper, etc., often, also, produces great relief. Weak infusions of tobacco, in the form of enemata, which were recommended by Saunders and Craigie, are said to give results similar to those obtained by belladonna.

By the side of the narcotics stands chloroform, as a remedy for the relief of pain and spasm. It is either given internally, in doses of one to two grammes, in capsules, etc., or in the form of inhalations, when we have to deal with an especially severe attack. It needs no further discussion that all the precautions must be adopted, and that all the dangers are present which are connected with the use of chloroform inhalations in surgery. Under certain circumstances the chloroform may be superseded

by chloral. It must be left to the judgment of the physician to determine when it should be employed.

In the very beginning of the attack the patient, if the surroundings permit, should be placed in a lukewarm, full bath, in which he should remain as long as possible, at least half an hour. Then (or instead of the bath) warmth should be employed in the form of fomentations, hot poultices, warm flannels, etc., to the painful hepatic region. Many patients, however, resist such applications, because the restlessness and pains are too severe; but we must insist upon them, as considerable relief is almost always produced immediately afterward. All patients do not tolerate the local application of heat, whereas, on the other hand, cold is sometimes soothing. According to Brichetau's plan, the liver and corresponding portions of the back are covered with an ice-bag, or so-called ice-poultices are used instead, chopped ice being mixed with dry flax-seed, and enclosed in linen, like a poultice.

Strong sinapisms, inunctions with opium and belladonna ointment, and similar local measures, often produce considerable relief of the pain.

The best results are also attained, at times, by permitting the patient to drink large quantities of hot water, to which five to ten grammes of bicarbonate of soda are added. According to Prout, who first recommended this plan, not alone the annoying symptoms of excessive acidity of the stomach are removed in this manner by the alkali, but the hot water also acts directly like a hot fomentation upon the organ which is the seat of pain. The first portions of the water are usually rejected immediately, but the stomach is soon relieved, the patient retains the water, and, as a rule, the pain subsides. A further advantage of this method consists in the fact that the water relieves the violence of the vomiting, which is usually very severe, and may even prove dangerous to the patient when the stomach is empty. However, narcotics are not rendered superfluous by this plan. It is useful to add a few drops of tincture of opium to the alkaline water, after the latter has been vomited once or twice (Murchison).

The emesis which occurs during the attacks of colic demands no special treatment, if the contents of the stomach are merely evacuated. But when the vomiting is repeated very fre-

quently, and is very severe and painful, not only is the strength of the patient exhausted, but there is also danger of a rupture of the dilated gall-bladder and the gall-ducts, and this symptom must, therefore, be treated. We should allow the patient to swallow small pieces of ice, and administer small quantities of champagne, effervescing drinks (pulvis aërophorus, etc.).

Local bleeding is indicated when marked evidences of inflammatory irritation of the liver and biliary passages, of congestion, etc., are present. When the region of the gall-bladder is very sensitive, or even marked and continuous pains are observed in it, and the attack of colic has persisted for a long time, great relief is often experienced from the application of a few leeches to the right hypochondrium. On the other hand, we cannot expect much benefit from general venesection. At all events, we should not, as was formerly the custom, perform this operation in every attack, in order to relieve the spastic impaction of the concretions, although this effect is often obtained. However, venesection may become necessary in plethoric individuals, with excited heart's action and severe cerebral congestion, before we pass to the employment of narcotics and other sedative remedies.

When the pulse becomes feeble, when syncope, coldness of the extremities, and other symptoms of weakened action of the heart, appear, excitants and stimulants are indicated, such as wine, ether, musk, liq. ammon. anisat., swathing in hot cloths, mustard poultices to the calves, friction with flannel, rubbing the skin, etc.

General reflex spasms demand similar treatment; in addition, we may also resort to cautious inhalations of chloroform.

When the pain has disappeared, and the paroxysm proper is over, many physicians employ mild purgatives, especially the "bitter waters" (Friedrichshall), castor-oil, infusion of senna, etc., in order to clear the bowels and remove the concretions. Others abstain from this plan, because they believe that purgatives are of little value under such conditions, and readily exhaust the patient, who is already weakened from the paroxysms. But purgatives are often necessary after the termination of the attack, in order to obviate the constipating action of the opiates,

and to relieve the hepatic congestion to which such patients have a great tendency.

Moreover, various substances to which, in part, a specific action against hepatic colic has been attributed have been recommended as antispasmodic remedies, which further the movement of the calculi in the bile-ducts, such as calomel with scammony and rhubarb (Saunders), sulphate of soda (Pujol), and tartar-emetic (Bright). Recently, podophyllin has also been added to these remedies, but it appears to be less employed in Germany than in England, France, and Italy. Mercadié reports (Le mouvement médical, 1877, No. 30, p. 328) his experience with this remedy, which he was induced to use by the favorable results communicated by Bufalini in the Florentine Lo sperimentale. The latter[1] saw rapid disappearance of the hepatic colic under small doses of podophyllin (0.01 grm. daily). In one case he continued the administration for an entire year without seeing any bad results. The colic did not again appear, although two years had elapsed. In another case of hepatic colic, against which the most varied remedies had been useless, Bufalini administered 0.01 grm. podophyllin daily, and saw rapid disappearance of the colic and calculi. After the remedy was discontinued, good health persisted for eight months; the hepatic colic then again appeared, but was relieved almost immediately by the renewed use of the remedy. Mercadié had a similar experience; in several cases he observed the passage of calculi in the stools during the podophyllin treatment.[2]

Special attention must be paid, in hepatic colic, to emetics as antispasmodics. Good results have been obtained from the administration of tartar-emetic in nauseating doses, but the use of emetics proper should be avoided, because the severe concussion

[1] According to Van den Corput, podophyllin is very serviceable in congestion of the liver. When introduced into the duodenum of dogs, it considerably increases the secretion of bile, and the latter is richer in solid constituents than usually.

[2] *Kochler* also recommends podophyllin in gall-stones and constipation. *Vide* Allg. med. Centralztg., XLVII., 1878, S. 94. According to Horace Dobell (British Med. Jour., June 14, 1879, p. 892), the drug should not be given in pill form, as is usually done, but as tincture (0.12 grm. podophyllin to 8 essent. zingib. and 60 spir. vin. rect.) One teaspoonful of this tincture is given in a wineglassful of water before retiring every day, or once in two, three, or four days.

and friction of the viscera in vomiting may readily lead to rupture of the occluded bile-ducts, and because, when cholecystitis or cholangitis happens to be present, rupture of the ulcers, perforation of the gall-bladder or the bile-ducts may occur. It would be more advisable to use emetics in cases in which jaundice continues after all other symptoms of the hepatic colic have been removed, and in which, therefore, a gall-stone is permanently impacted in the ductus choledochus. Here they may serve to dislodge the stone and to favor its expulsion, but we must premise that the greatest caution is to be observed, and that the cases must be of such a nature that no symptom indicates inflammatory irritation of the bile-ducts. When the utility of emetics is so restricted, it is understood why many entirely disapprove of their employment in cholelithiasis (Bamberger).

When the symptoms of closure of the choledochus persist after the attack of colic, the expulsion of the occluding concretion must be favored by stimulating the peristaltic movements of the intestines. Apart from emetics, we may employ for this purpose purgatives, ethereal inunctions and frictions of the abdomen, warm baths, and especially also the alkaline mineral-waters of Carlsbad, Ems, Kissingen, Fachingen, Vichy, etc., because these, as is well known, produce increased secretion of bile, and the stronger flow of this fluid may carry the stone into the intestines by purely mechanical means.

All other manifestations of cholelithiasis, such as inflammations of the biliary passages and their extension to the peritoneum, the liver, and the portal vein—furthermore, the perforation of the bile-ducts and the formation of free or encapsulated extravasations of bile, the permanent retention of calculi in the biliary passages, and occlusion of the latter, the ileus produced by large gall-stones, etc., must be treated according to general principles, and demand no special remarks. The treatment of almost all these conditions is, in the main, symptomatic, and antiphlogosis occupies the foreground.

We reiterate, with regard to the intermittent fever occasionally produced by calculi remaining in the hepatic ducts and ductus choledochus, that it must be treated like idiopathic intermittent fever, and that quinine is effective against this symptom.

The idea of combating permanent occlusion of the excretory ducts by surgical operations has, at various times, been either merely referred to or discussed in a definite shape (J. L. Petit, 1743; Thudichum, 1863; Marion Sims, and others, 1878), and very recently especially among English physicians. These discussions have hitherto led to no results; positive proposals and more accurate indications are still wanting in this direction. The achievements of surgery in cholelithiasis are restricted to the field of cutaneous biliary fistulæ and cholecystitis calculosa. The most important data with regard to the last mentioned affection and cholecystotomy are found in the section on dilatation of the gall-bladder (*vide* page 647).

The second chief object of treatment in cholelithiasis consists in the solution of the concretions which may still be present in the biliary passages, and in preventing the formation of new calculi. At the present time it is very generally held that the idea of dissolving gall-stones within the biliary passages by means of certain remedies is based upon a therapeutic illusion. But be the effect of the remedies under consideration what it may, be the theory upon which their action is explained what it may, there is a general unanimity of opinion among practitioners that the substances in question exert a favorable influence upon the removal of the cholelithiasis.

The solubility of these concretions, which are chiefly composed of cholesterine (and these constitute by far the greatest proportion), in ether, chloroform, alcohol, and ethereal oils, necessarily led to the presumption that these substances produced a similar action upon the concretions in the living organism. Durande's remedy—which was discovered toward the end of the last century, was for a long time regarded as a specific lithontripticum, and is, even at the present time, employed by many physicians—depends upon this presumption. It consists of a mixture of 3 parts æther sulphur. and 2 parts ol. terebinth. According to the original prescription, the patient should take 4 grm. of the mixture every morning until 500 grm. have been taken. The remedy is, however, rarely tolerated in such large doses; it is more advisable to give 20–30 drops two or three

times daily. As the Durande remedy is disagreeable to take, and is not well tolerated, Soemmering advised that the ether alone be employed mixed with the yolk of egg, and Duparcque recommended the mixture of ether with castor-oil. It needs no extended remarks to prove that Durande's remedy cannot effect a solution of the calculi in the living organism. This had been shown by Thénard, who attributed the undeniable good effects of this remedy in cholelithiasis to the antispasmodic action of the ether. As ether and similar remedies are rapidly absorbed by the gastric mucous membrane, and immediately pass into the portal vein, many physicians adhere to the opinion that a sufficient amount of ether, etc., may be mingled with the bile surrounding the concretions, in order, after prolonged use of the remedy, to gradually change the calculus superficially, to loosen its strata, diminish its circumference, and perhaps prepare the way for its disintegration. Whether this view is correct or not, there is no doubt that ethereal substances are used by preference against cholelithiasis by many physicians who reject the notion that they are able to dissolve the concretions.

Frerichs, on the other hand, states that it is best to discard these remedies entirely, because their solvent action does not come into play, and their antispasmodic effects are surpassed by those of morphine and other narcotics.

Instead of the Durande remedy, the internal use of chloroform has, in recent times, been resorted to as a solvent. This suggestion was originally due to Bouchut, and appears to have met with special favor in America.[1]

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[1] *Buckler* (Bost. Med. and Surg. Journ., Oct. 23, 1879) maintains that calculi may be dissolved in the gall-bladder as readily as in a test-tube. Five to sixty drops of chloroform taken internally every four to six hours is said to be a certain method of dissolving even large and numerous stones. Most patients, however, cannot absorb more than ten to fifteen drops every four to six hours by the stomach. In this event the remedy must be administered continuously for at least two to three weeks. Instead of chloroform, chloral may be given, which produces its effect as nascent chloroform. *Buckler* (Amer. Journ. of Med. Sc., 1867) also advises succinate of iron instead of chloroform, or, in urgent cases, in addition to it. *Octerlony* (Trans. of Med. Soc. of Kentucky, 1877) reports favorable results in cholelithiasis from the use of succinate of iron. These remedies would also act as solvents of impacted gall-stones, especially in closure of the choledochus, and thus prove a true radical cure.

Other remedies are rarely employed as specifics for the solution of calculi, and no reliance can be placed upon them. To this class belong electricity (employed by Hall, of Philadelphia, in 1821), nitric acid, chelidonium, oxalic and phosphoric acids.

Gallic acid salts must also be mentioned here. M. Schiff (Gaz. hebdom., 1873, No. 15) prescribes 0.50 gramme at a dose of gallate of soda, in order to prevent the formation of cholesterine calculi, but denies that previously existing gall-stones are dissolved by it. Dabney[1] recommends the cholate of soda up to five grammes twice a day, in order to prevent the formation of fresh calculi.

Although theoretically obscure, the influence of alkalies upon cholelithiasis is practically beyond a doubt, both upon the removal of those gall-stones which are present as well as upon the development of fresh ones. The fixed alkalies were already regarded by Fr. Hoffmann, of Halle, in the beginning of the last century, as a solvent for calculi. It has been proven that cholesterine and cholepyrrhinlime—*i.e.*, the chief constituents of almost all gall-stones—are dissolved by strongly alkaline bile, which, on the other hand, is naturally destitute of influence upon those rare forms of calculi which are provided with a coating of lime. As, in addition, a thin, watery bile will favor the loosening of the stones, and their mechanical destruction, we can understand why alkalies have been so often employed in cholelithiasis, especially in the form of alkaline mineral-waters. These have proven themselves by far the best remedy in cholelithiasis. Thousands of patients return from these watering-places cured, or have recovered at home by the aid of the waters. Whether the alkaline mineral-waters have a direct chemical action (solution) upon the gall-stones in the organism, is problematical to a high degree. There is no doubt, however, that they increase the secretion of bile, and restore the normal condition of the secretory apparatus.[2] The calculi are more readily

[1] The Use of Cholate of Soda to Prevent the Formation of Gall-Stones (Amer. Journ. of Med. Sciences, April, 1876).

[2] *Vide* also the investigations of *Rutherford* and *Vignal* (British Med. Journ., 1877), concerning the cholagogue action of various remedies, which were made upon dogs with biliary fistulæ. Cholagogue action was manifested, among others, by large doses

carried off (often without being noticed) by the copious flow of thin bile. The calculi are found in the stools, as a rule, uninjured, sometimes destroyed, and only exceptionally with signs of chemical action (?) (*vide* page 704). How great a share is taken in the treatment of cholelithiasis by the water used to dilute the alkalies, is evident from the physiological experience that the increased ingestion of water by animals produces a greater secretion of thin bile. And the statement is very plausible, that individual cases of cholelithiasis have been relieved by copious draughts of water (Vanotti). Moreover, there can be no doubt that alkaline mineral-waters benefit the general health, remove the tendency to acid formation in the stomach, diminish hepatic congestion, and produce such changes in the constitution of the bile that the chances of renewed calculus formation are diminished.

Among the alkaline waters, those of Carlsbad and Vichy lay claim to the most brilliant results. Then follow those of Ems, Kissingen, Homburg, Marienbad, Fachingen, Contrexéville, Vals, etc.

In the choice of one of the above-mentioned watering-places the individuality of the patient is decisive. Carlsbad undoubtedly takes the first rank as the most effective water, and its rival, Vichy, approaches it very closely with regard to efficacy. While Carlsbad deserves the preference in cases which are associated with obstinate constipation, Marienbad is indicated in plethoric individuals inclined to congestions, and Ems in irritable, weakened patients with a tendency to diarrhœa. As a rule, the drinking cure proper is combined with the use of lukewarm alkaline baths. In order to render success certain, it is extremely desirable to repeat the cure several times. Patients who have followed out this plan for two consecutive seasons are said, according to the experience of Willemin, to present an immunity against relapses of cholelithiasis lasting several years.

When we are forced by the circumstances of the patients to resort to alkaline drugs instead of the corresponding mineral-waters,

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of sulphate of soda (not sulphate of magnesia), sulphate of potassa, and phosphate of potassa (not by carbonate or bicarbonate of soda). Chloride of ammonium was inert.

bicarbonate of soda should be administered, either alone or combined with sulphate of soda, in a large amount of water. In this form it interferes less with digestion, apart from the fact that we have learned to regard the large quantity of water as an essential factor in the curative properties of alkaline mineral-waters in cholelithiasis. When bicarbonate of soda is used for a long time, the addition of laxative salts should be discontinued, in order to distress the digestive organs less; in its stead we may employ a mild infusion of rhubarb.

Instead of the alkaline carbonates, Bouchardat has advised the use of vegetable acid alkalies (acetic and citric acids).

Those herbs, also, whose efficacy depends chiefly upon their proportion of vegetable acid alkalies, and grape-cures, have been recommended in cholelithiasis. However, they are only tolerated by such individuals whose stomach is in good condition.

Among the older physicians, the bitter vegetable extracts stood in good repute against cholelithiasis. They are very rarely employed at the present time, because they only have any perceptible effect when freshly prepared and taken in large quantities, and because they cannot be compared with the alkaline medication, which is as agreeable as it is certain.

It is of the greatest importance in all cases that the patient should adopt a proper regimen. He must rise early, exercise considerably in the open air, sleep in a well-aired room, be moderate in eating and drinking, avoid the use of wine and alcoholic drinks as much as possible, and abstain from all fatty and saccharine articles of diet and from malt drinks. The greatest care must be paid to the regulation of digestion and the intestinal functions, and the prevention of constipation or diarrhœa. Exposure and excessive bodily exertion should be avoided. All these rules must be followed out with special strictness in women at the period of menstruation.

DISEASES OF THE PORTAL VEIN.

Historical Sketch.

The portal vein bore an extremely bad reputation among the older physicians. It was regarded as the starting-point for numerous diseases of all kinds. Vena portæ porta malorum . . . . says Stahl (1698). This opinion, however, was not the outcome of positive anatomo-pathological investigations, but was rather the result of theoretical prejudices. The want of a clear insight into the physiology and pathology of the liver, the blood, etc., had, as a consequence, that this gap was filled by speculations which were often of a "vitalistic" character. Only very gradually did the view obtain that many disorders, whose location had been attributed, in consequence of a deep-seated prejudice, to the portal vein, must be regarded as due to diseases of the liver, intestinal canal, lungs, and heart. However, a positive rupture with the speculative "portal vein pathology" of Stahl, Boerhave, van Swieten, Kämpff, and others, only occurred toward the end of the last century, when the study of phlebitis and of diseases of the vessels (which is, in many respects, the groundwork of pathology) began under the auspices of John Hunter.

In Germany, the work of Sasse (de vasorum sanguiferorum inflammatione, Halæ, 1797) first "opened the ball" in this cause. As a matter of course, the progress in our knowledge of phlebitis aided our insight into the character of diseases of the portal vein. However, almost all our positive knowledge and our really useful data in this respect are the fruit of the present century.

As with phlebitis in general, so also with regard to inflammatory processes of the portal vein, we first became acquainted with

their anatomical aspects, viz., thrombosis, the various metamorphoses of thrombi, their puriform degeneration, and suppurative pylephlebitis (the latter through Sasse). As the founder of the clinical study of pylephlebitis[1] we must mention Schoenlein (1830), who was also the first to diagnose suppurative pylephlebitis during life. The doctrine of inflammation of the portal vein has, moreover, passed through all the changes which were experienced by phlebitis in general. The mistaken idea that the coagulation of blood in the vein was the expression of inflammation of the vein, *i.e.*, the identity of thrombosis and phlebitis, also dominated, for a long time, the doctrine of inflammation of the portal vein, and gave rise to many obscurities and wrong notions, the consequences of which are noticeable until recent times. Only since Virchow investigated the relations of thrombosis and inflammation of vessels and has shown the causal connection between both processes (inasmuch as he recognized thrombosis as one of the most frequent causes of phlebitis and clearly showed the causal relations of phlebitis and thrombosis in all directions), has full light been shed upon our knowledge of pylephlebitis. Credit is also due to Frerichs, inasmuch as he investigated the clinical aspects of diseases of the portal vein, based upon Virchow's doctrine of phlebitis. The characters which this study assumed under his hands will hold good approximately even at the present time. Nor can the services of both of these men be lowered by the remark that the doctrine, as it stands, would have resulted of itself. It is an attribute of genius that it finds the proper expression for a truth which is "in the air" and which would be proclaimed by every one could he but find the proper terms.

The changes, in the most recent times, with regard to the previously dominant interpretation of the nature of diseases of the portal vein, especially of suppurative pylephlebitis, refer to the distinction which we have learned to make between non-specific inflammations and infectious mykotic processes. Not alone do certain peculiarities in the character and course of the above-mentioned disease appear more comprehensible from a consider-

[1] The term pylephlebitis was first employed by *Messow*. *Vide* his dissertation: De inflammatione venæ portarum s. pylephlebitide. Berolini, 1841, S. 6, Anm.

ation of these factors, but a clearer light is also thrown upon the relations of suppurative pylephlebitis to pyæmia and to metastatic abscesses of the liver, which were hitherto rather indefinite and therefore often remained unconsidered.

Anatomical and Physiological Remarks concerning the Portal Vein.

The portal vein collects the venous blood of the chylification organs (stomach, intestines, spleen, and pancreas) in order to carry it to the liver, where it undergoes further change. Its trunk has a diameter of about 1.4 centimetre and a length of five to eight centimetres. It arises in the region of the head of the pancreas by the union of the splenic vein (which runs horizontally from the left) and the much larger vena mesenterica superior which ascends in a curved line. The inferior mesenteric vein, which arises from the rectum and left colon, enters at the right angle, under which the above-mentioned veins unite, or it may pass into the superior mesenteric vein. In addition, the trunk of the portal vein (or the superior mesenteric) also receives the small pancreatico-duodenalis vein and the superior gastric vein from the lesser curvature of the stomach. The trunk of the portal vein lies in the right half of the abdominal cavity, not far from the median line of the body, and is nowhere in apposition with the abdominal walls. Enclosed within both ligaments of the hepatico-duodenal ligament, and accompanied on the left side by the hepatic artery, on the right by the common bile-duct, the portal vein ascends to the transverse fissure of the liver, and, therefore, approximately pursues the same direction as the inferior vena cava, except that it passes, at the same time, a little from the left to the right. The opening of the lesser omentum is situated between the vena cava and the portal vein. If the finger is introduced through the opening of the cavity of the omentum, the foramen Winslowii, it lifts up, at the same time, a strand as thick as the thumb, which includes the portal vein, hepatic artery, ductus choledochus, the plexus nervos. hepaticus, and a number of lymphatics—all of which are united to-

gether by the so-called Glisson's sheath, and are enclosed by the serous layers of the hepatico-duodenal ligament.

In front of the transverse fissure, the portal vein divides into two chief branches for the right and left lobes of the liver. Under continuous dichotomous division they finally end in the terminals, or the so called interlobular veins, from which the capillary system of the hepatic lobules originates. From the capillaries of each acinus the blood is then carried by the so-called vena centralis lobuli into the hepatic veins, and from the latter into the inferior vena cava. In addition, there are direct communications, within the liver, between small branches of the portal vein and the hepatic veins, by which anastomoses, a small portion of the blood of the portal vein is conveyed directly into the hepatic veins without passing through the capillary system of the hepatic lobules. Fr. Aug. Walter[1] had recognized these anastomoses, but a knowledge of them then became forgotten, until they were again discovered by Claude Bernard.[2] Many of them are fine veins, which, like the radicles of the portal vein proper, take their origin from the digestive organs and carry their blood, not into the trunk of the portal vein or its branches, but pass independently into the liver, usually in the vicinity of the transverse fissure. They are termed accessory portal veins (this term is also applied to another category of veins).

The circulatory system of the portal vein is not by any means completely closed in itself, but communicates in various places with the system of the vena cava. As a rule, however, these communicating branches are poorly developed and only include small vessels. In case of necessity, however, when the blood cannot escape through the portal vein, these anastomoses may be strongly dilated, so that a collateral circulation[3] is estab-

[1] *Vide Luschka*, Anat. d. menschl. Banches, Tübingen, 1863, S. 338.

[2] Comptes rendus, 1850, XXX., p. 694.

[3] The flow of the blood of the portal vein into the territory of the vena cava, under such circumstances, occurs chiefly by means of vessels which are normally present, but also in part by new-formed ones. *Kiernan* has shown, with regard to the latter, that the new-formed fine veins in the false membranes, between the upper surface of the liver and the diaphragm, permit the escape of blood from the veins of the capsule of the liver (territory of portal vein) to the venæ diaphragmaticæ (territory of vena cava). This collateral circulation could hardly, however, be of any special service.

lished by means of which the blood, which should flow through the portal vein, is carried through the system of the superior, and especially the inferior, venæ cavæ to the heart.

Among the normal channels of communication between the systems of the portal vein and vena cava,[1] special attention must be paid to the radicles of the superior gastric and inferior mesenteric veins.

The superior gastric vein receives its supply from the region of the cardiac orifice and the lower portion of the stomach. But these radicles also anastomose[2] with the inferior œsophageal veins, which communicate with the intercostal veins and vena azygos, and also with the superior and inferior diaphragmatic veins, which pass to the superior and inferior venæ cavæ.

There is a still freer communication between the systems of the vena porta and cava through the plexus which surrounds the rectum, as the superior hemorrhoidal veins empty into the inferior mesenteric and portal veins, and the inferior hemorrhoidal into the internal pudendal and hypogastric veins—*i.e.*, into the inferior vena cava.

In addition, small veins are inserted between the systems of the vena portæ and vena cava. Although these arise in the intestinal walls, they do not empty into the portal vein, but pass by a small branch sometimes directly into the inferior vena cava, sometimes into one of its branches.[3] Especially do a number of these small vessels pass from the duodenum and colon to the vena cava.[4]

In addition, Sappey's system of accessory portal veins must also be taken into consideration. These are vessels which originate in organs other than the intestine and its annexes, and which

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[1] *Sappey* has investigated this subject: Recherches sur un point d'anatom. path. relatif à l'histoire de la cirrhose. Mém. de l'acad. de méd., XXIII., p. 219, and Bulletins de l'acad. de méd., 1859, T. XXIV.

[2] The communication in question had been recognized by *Haller*.

[3] These anastomoses were discovered by *Retzius*, *Tiedemann*, and *Treviranus*: Ztsch. f. Phys., Bd. V., 1833.

[4] *Rindfleisch* (Path. Gewebelehre, 2 Aufl., S. 420) found the branches of the portal vein in the liver closed in a case of cirrhosis. The blood entered directly with the veins of the internal spermatic plexus into the inferior vena cava through a number of anastomoses with the mesenteric veins.

pass directly into the liver or into the portal vein immediately before its entrance into the liver. Of the five groups of accessory portal veins described by Sappey, we are specially interested in two, viz. : the veins of the suspensory ligament of the liver and the vena parumbilicalis.

The former originate in the depth of the diaphragm, descend in the suspensory ligament, and are distributed to the hepatic lobules in the vicinity of the former. They communicate on the one hand with the diaphragmatic veins, and through these with the venæ cavæ, and on the other hand with those hepatic branches of the portal vein which correspond to the arteries of the capsule of the liver. As a rule, these veins are very small, but Sappey on one occasion saw ten to twelve veins start from the convex surface of the liver and ascend in the suspensory ligament to the diaphragm. Three or four of these were as thick as ravens' quills.

The vena parumbilicalis, a term applied to this vessel by Schiff,[1] is more important. The anastomosis, which was discovered by Burow[2] (1838) in the fœtus, between the portal vein or the end of the umbilical vein, and the system of the inferior vena cava, has been recognized by Schiff as occurring in adult life; it is identical with the vena parumbilicalis. The radicles of the latter originate in pairs on each side from the external iliac and epigastric veins. They unite in the neighborhood of the umbilicus into a single trunk, and receive a few fine branches from the fundus of the gall-bladder.[3] The vena parumbilicalis then ascends from the umbilicus next to the round ligament of the liver, receiving small branches from the peritoneum and the recti muscles, and empties into the portal vein at the point where the termination of the obliterated umbilical vein unites with the lat-

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[1] *Schweizer*, Ztschr. f. Heilk. Bern., 1862, Bd. I.

[2] Müller's Arch. f. Anat. u. Phys., 1838, S. 44.

[3] A few branches of the parumbilical group of veins are provided with valves, the concavity of which is directed toward the heart (*Henle*). According to *Schiff*, the vena parumbilicalis not alone serves to carry the blood of the portal vein into the vena cava (through the subcutaneous veins of the abdominal walls, the epigastric and internal mammary veins), but also in obliteration of the trunk of the portal vein, to carry a sufficient amount of blood to the hepatic branches of the latter.

ter. If the portal circulation in the liver is disturbed or entirely interrupted, but the trunk of the portal vein is permeable, the vena parumbilicalis is sometimes found dilated to the thickness of a finger. It then appears to be the direct continuation of the trunk of the portal vein, whose blood it carries through the umbilicus into the veins of the anterior abdominal walls. Cruveilhier, who described a case of this kind with an enormous development of the so-called "medusa head" in the abdominal walls, of which he made an admirable drawing (*vide* his Atlas of Path. Anat., livr. 16, pl. 6), was led by the thickness of the vena parumbilicalis to regard it as the umbilical vein itself.[1] Henle (Gefässlehre, S. 371) and others were able to satisfy themselves in such cases that the obliterated umbilical vein was present as usual, in addition to the vena parumbilicalis, which was as thick as a finger.

As a matter of course, the various anastomoses between the system of the portal vein and that of the vena cava possess a variable significance, both physiologically and pathologically. This significance depends upon the constitution of the blood which they contain, or upon the territory from which their radicles derive blood; furthermore, upon the direction in which the fluid within them flows, and (this is dependent thereon) especially upon the situation of those portions of the territory of the portal vein, in the concrete case, which are permeable or impermeable. It does not, therefore, appear advisable to formulate, in general terms, the physiological significance of these anastomoses.

The portal vein is exactly similar to the other veins in the body in its finer structure as well as its capacity of undergoing various forms of disease. The radicles, trunk, and the hepatic

[1] *Ménière* (Arch. gen. de méd., 1826) saw in an individual, æt. twenty-five years, who died of meningitis, a vein as thick as the index finger, which was given off at a right angle from the lower and inner part of the right iliac vein, passed along the upper edge of the pubes to the symphysis, and then upward behind the linea alba. From the umbilicus it ascended at the posterior edge of the falciform or suspensory ligament of the liver, and finally emptied into the dilated sinus venæ portæ. This vein possessed valves which opened toward the heart. The upper part (inclosed in the suspensory ligament of the liver) appeared to be the umbilical vein itself. A similar case was described by *Manec* (Recherches Anat.-pathol. sur la hernie crurale, Paris, 1826).

ramifications of the portal vein are all destitute of valves. The blood flows in the portal vein under very slight pressure and with slight rapidity. Stasis of blood in its territory therefore occurs very readily, giving rise to ectasia, dilatation, and sinuosity of the vessels and to coagulation of the blood contained in them. In addition to the slight *vis a tergo*, the respiratory movements furnish a considerable portion of the power which propels the blood in the portal vein; inspiration acts as a suction force, and increases the rapidity of the current in the portal vein, while expiration increases the pressure, and therefore causes diminution of the rapidity. Fixation of the right half of the diaphragm in affections of the pleura, etc., must therefore permanently interfere with the flow of blood in the portal vein.

The physiological properties of the blood of the portal vein require less consideration for our purposes. We are more interested in the relations of the terminal branches of the hepatic artery and the branches of the portal vein in the liver, together with the connections existing between the two, because thereon depends the possibility of an establishment of equilibrium between the two when one or the other has been occluded. At the present time we only refer to those cases in which the occlusion affects the trunk of the portal vein or one of its large branches. In such an event, it is a remarkable fact that the liver is often found unchanged or but slightly hypertrophied, even after prolonged duration of complete occlusion of the vessel. We know from the investigations of Cohnheim and Litten[1] that the interlobular terminations of the hepatic artery empty only in very small part into the capillary meshwork of the acini. The hepatic artery chiefly nourishes those tissues which are situated in the interlobular spaces, and the small veins which collect the blood from the capillaries of these spaces empty into the interlobular branches of the portal vein. In occlusion of larger branches, or even of the trunk of the portal vein, the hepatic tissue receives, through the medium of the open interlobular veins, sufficient blood from the (often dilated) hepatic artery to nourish it, although, as a matter of course, the functions of the liver,

[1] Ueber Circulationsstörungen in der Leber, Virch. Arch., Bd. 67, S. 153 (1876).

under such circumstances, will be correspondingly diminished. Only when the interlobular veins become impermeable, as so often occurs in cirrhosis, is the supply of blood to the capillary system of the hepatic lobules interrupted, and atrophy of numerous acini occurs, because the hepatic artery can convey no blood to the capillaries of the acini after the closure of the interlobular veins.

Thrombosis and Occlusion of the Portal Vein.

(Pylethrombosis.—Pylephlebitis adhesiva, P. chronica.)

Bouillaud, Arch. gén. de méd. T. II., 1825.—*Reynaud*, Journ. hebdom., 1829.—*Stokes*, Lectures on the Treatment of Internal Diseases, German by Behrend. Leipzig, 1839.—*Carswell*, Illustrations of the Elementary Forms of Diseases. London, 1838 (Art. Atrophy, Pl. II., Figs. 4 and 5).—*Cruveilhier*, Anat.-pathol. Atlas, Livr. XVI., Pl. 6 (Medusa head).—*Stannius*, Ueber krankhafte Verschliessungen grösserer Venenstämme d. menschl. Körpers. Berlin, 1839.—*Puchelt*, Das Venensystem in seinen krankhaften Verhältnissen. 2 Aufl. Leipzig, 1844.—*Schuh*, Ztschr. d. Ges. d. Wiener Aertze, 1846, II., S. 353.—*Monneret*, Union méd., 1849, p. 49.—*Gintrac*, Observat. et recherches sur l'oblitération de la veine porte. Journ. méd. de Bordeaux, 1856 (Schmidt's Jahrb. d. ges. Med. Jahrg. 1857, Bd. 93, 94).—*Frerichs*, Klinik d. Leberkrankhtn. Braunschweig, 1861. II., S. 363.—*Ziegler*, De venæ portæ obstructione. Diss. Königsberg, 1860.—*Botkin*, Krankheitsgeschichte eines Falles von Pfortaderthrombose. Virch. Arch., Bd. 30, S. 449 (1864).—*Alexander*, Thrombose der Pfortader u. ihre Aeste. Berl. klin. Wschr., 1866. No. 4 (Virch. u. Hirsch. Jahresber. f. 1866, II., S. 82).—*Leyden*, Fälle von Pfortaderthrombose. Ibid., 1866, No. 13, u. Jahresber., S. 83.—*Pippow*, Ueber die Obturation der Pfortader. Diss. Berlin, 1868.—*Payne*, Thrombosis of Portal Vein: Trans. of Path. Soc., Vol. XVI., p. 228, 1871.—*Habershon*, Occlusion of Vena Portæ, etc. Guy's Hosp. Rep., 1871.

The names mentioned in the caption do not, by any means, refer to identical diseased processes. Thrombosis of the portal vein, in general, goes hand-in-hand with occlusion of the vessel, but stenosis of the portal vein of high degree with the symptoms of occlusion of the vessel is conceivable without pylethrombosis, although, in reality, it is very rarely observed without the latter. In addition, pylethrombosis does not by any means cover the

conception of adhesive pylephlebitis. Although the latter disease necessarily presupposes a coagulation of blood in the portal vein, the term "adhesive pylephlebitis," in its strict sense, is only applicable to those (rarer) cases of pylethrombosis in which organization of the thrombus has occurred, with organic occlusion of the vessel and its transformation into a solid connective-tissue cord. The common factor, therefore, in the above-mentioned diseases is not of an anatomical, but of a physiological or functional nature ; it consists in the interference with circulation, and in the impermeability of the vessel.

The beginning of our knowledge of thrombosis of the portal vein and of the inflammation of this vessel dates back to a period in which the "phlebitis" theory of John Hunter had secured general recognition. According to this theory, the coagulation of blood within the vein was regarded as a sign that an inflammation of the walls of the vein was present. In applying this doctrine to the portal vein, two forms of inflammation of this structure were distinguished : one was characterized by the coagulation of blood, the other by the presence of pus in the vessel. These forms were regarded as terminations of one and the same inflammatory process. The former was termed adhesive, the latter suppurative pylephlebitis. With regard to the character of its course, the former was called chronic, the latter acute pylephlebitis. In short, simple closure of the portal vein from thrombosis was mistaken for a much more serious affection, viz., true (purulent) inflammation of the portal vein, and the very distinct features of each disease therefore lost some of their clearness, on account of the constant tendency to mistake one for the other.

A clear insight into the nature and mutual relations of both diseases was obtained by the application of Virchow's doctrine of thrombosis and phlebitis to the diseases of the portal vein. According to this doctrine, we may consider it settled with regard to the portal vein, as well as the veins in general, that thrombosis, in the majority of cases, occurs independently of an inflammation of the walls of the vein, that it often leads to a condition of inflammation in the affected vein (of a slight grade and chronic course), and that, on the other hand, in only very rare

cases do certain primary diseases of the wall of the vein give rise to coagulation of the blood, and thus to thrombotic occlusion of the portal vein. Cases of the latter kind may, under certain circumstances, develop in such a manner that they approach true (suppurative) pylephlebitis, and thus form the connecting link between the two diseased processes.

It is not always easy, especially in chronic cases, in which the wall of the vessel and its contents have undergone all kinds of changes, and in which secondary alterations of the most varied characters have supervened, to clearly define the connection between the phenomena, especially when the anatomical lesions are not accurately described, as is so often the case in observations dating back to an early period. The general pathology of thrombosis and phlebitis, in the form handed down to us by Virchow, will then afford a reliable basis. We must, then, sift an obscure case with regard to the connection of the phenomena by the aid of the general principles.

Etiology.

As is well known, Virchow has divided the thrombi, which form in veins having healthy walls in consequence of mere retardation of the current of blood, into four groups, according to their underlying causes, viz., thrombosis from compression, dilatation of the vessels, and marasmatic and traumatic thrombosis. Of these four varieties only the compression and marasmatic thromboses occur in the portal vein. Traumatic thrombosis of the portal vein, except in its finest branches and radicles, is scarcely conceivable, because injuries of the trunk or larger branches of the vessel are not alone very rare, but would soon lead to death from hemorrhage. Dilatation thrombosis does not occur, at least in its pure form, in the territory of the portal vein, because, in addition to the dilatation, other factors, such as compression, weakness of the heart's action, etc., are also present, and may in themselves act as causes of coagulation.

General pathology teaches, furthermore, that thrombosis may also develop as the result of textural changes in the walls of the vessels. Such thromboses occur, indeed, in the portal vein, but

we will refer to them under the head of pylephlebitis, because those coagula of the portal vein, which are due to a disease of the wall (as a rule to inflammation), almost always present themselves with a history of suppurative pylephlebitis. We will, therefore, only deal with compression or marasmatic thrombosis.

Marasmatic thrombi occur very rarely in the vena porta when compared with those in other veins. That the weakness of the heart's action, and the consequent general retardation of the current of blood, are the origin of the occlusion of the portal vein, may be taken for granted, when local causes of the coagulation, such as diseases of the wall of the vein, affections of the liver or of the territory of the radicles of the portal vein, cannot be discovered, and when the weakness of the heart can be demonstrated. Both of the cases observed by Frerichs (l. c., II., S. 364) will serve as illustrations. Such thrombi usually occur only a short time before death, or even during the long-continued final agony. The thrombus—which usually involves not only the trunk and hepatic branches of the portal vein, but also extends, for a variable distance, into the large radicles (vena lienalis, mesenterica)—presents, therefore, a comparatively fresh appearance, and the sequences of occlusion of the portal vein often occur incompletely. On several occasions extensive coagula have also been found in other large vessels, viz., the pulmonary artery, superior vena cava, jugular vein (Frerichs), inferior vena cava (West, The Lancet, Feb. 23, 1878, p. 227).

Most cases of thrombosis of the portal vein belong to the category of compression thrombi. The immediate cause of the coagulation is, however, variable. Those cases are most frequent in which numerous vessels in the territory of the portal vein are destroyed, in consequence of certain diseased processes within the liver, and consequently stenosis and occlusion of the hepatic branches of the portal vein occur. The hepatic diseases in question are of a chronic character, and the thrombosis of the portal vein, therefore, develops very slowly. The thrombus has time to pass through the most varied metamorphoses, the sequences of occlusion of the portal vein, especially the changes in circulation, appear in their full development, and the resulting condition may continue for months, even for many years, until the

final termination. In these cases the occlusion is sometimes confined to the branches of the portal vein within the liver, sometimes the trunk and the large branches are occluded for a variable extent toward the periphery.

The most common exciting cause of this chronic form of pylethrombosis is the chronic atrophy of the liver in its higher grades, especially the simple (smooth) and the granular induration, or atrophic cirrhosis of the liver. The occlusion is sometimes incomplete and the vessel is only narrowed, or there is complete obturation. Reynaud (l. c.), Gintrac (l. c.), Frisson,[1] Dowel,[2] Monneret (l. c.), and many others, have reported cases of pylethrombosis in consequence of cirrhosis of the liver. It is remarkable that, in many of these cases, the walls of the portal vein were partially calcified (Gintrac, Frisson, Dowel). Frisson found the trunk of the portal vein, in a man aged fifty years, degenerated in its entire circumference, and converted into a rigid tube.

Other affections of the liver are much less frequent exciting causes of pylethrombosis than cirrhosis. Carcinomatous tumors of the liver have been found to lead to portal thrombosis.[3] But the thrombus is then usually confined to those hepatic branches which are directly compressed by the carcinomatous nodules, and it rarely assumes greater dimensions or even becomes general. Moreover, these occlusions after hepatic cancer usually last only a short time, and are similar, in this respect, to cases of marasmatic pylethrombosis.

Hepatic abscesses very rarely lead to coagulation of blood in the portal vein, and when this does occur the thrombus undergoes puriform degeneration, and the symptoms of suppurative pylephlebitis develop. It is well known, on the other hand, that hepatic abscesses often spread to the hepatic veins.

It is also of rare occurrence that the abnormally dilated biliary passages exercise pressure upon the portal vein, and thus lead to chronic inflammation and narrowing of the latter. An

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[1] Gaz. des hôp. 1848, p. 420.

[2] Dublin Quarterly Journ. of Med. Sci. 1851, Aug., p. 201.

[3] We only refer to occlusion by simple coagulation of blood. Carcinomatous thrombosis will be discussed at a later period.

observation of this kind was reported by Virchow;[1] this did not, however, refer to pylethrombosis, but to a marked narrowing of the lumen of the vessel by its thickened walls. But the case belongs in this category, inasmuch as the stenosis of the vessel is the essential feature of the disease under consideration.

In a man, æt. sixty-six years, suffering from melasicterus, ascites, and œdema of the feet, the liver was found atrophied, granular, and of a greenish color. The dilated gall-bladder was filled with numerous calculi. The cystic duct was wide and tortuous, as was also the ductus choledochus, whose markedly dilated terminal portion contained a round calculus as large as a musket-ball. In the portal vein the inner wall appeared thickened, in proportion as the vessel approached the liver, so that true stenosis of its lumen was produced. Toward the right lobe the internal wall was one centimetre in thickness, and appeared as a striated, semi-cartilaginous, dense mass, which was *calcified in great part, and only left a narrow channel for the current of blood.* On the left side the thickening was less considerable, although this also presented quite marked stenosis. Back of this the vessel was wide, the end of the trunk of the portal vein markedly dilated, and the walls thickened, so that it presented the appearance of arterial aneurism. The vena azygos was converted into a row of large sacs filled with blood, some of which reached to the vena lienalis, which also presented sacculated dilatations, three of which communicated with those of the vena azygos; an aneurismal varix was, therefore, present between the vena lienalis and vena azygos. Virchow attributes the primary obstruction to the flow of blood in the portal vein to the marked dilatation in the biliary passages, and surmises that the calculus, while situated higher up, produced a chronic inflammation of the wall of the portal vein by pressure, which, in its turn, caused occlusion of its lumen, etc.

The compression of the portal vein may occur without as well as within the liver, but the former happens more rarely. Such compression of the trunk of the portal vein is either produced by the retraction of inflammatory, new-formed connective tissue, or by tumors of various kinds. At times this only leads to stenosis of the trunk of the vessel, without coagulation of blood; at other times (and, indeed, as a rule) the compression causes complete occlusion by pylethrombosis.

Compression of the trunk of the portal vein, and stenosis of its lumen, with or without coagulation of blood inside the vessel, are occasionally seen as the result of chronic peritonitis. The latter is sometimes combined with hyperplasia of the connective

[1] Verhandlgn. d. phys. med. Gesellsch. zu Würzburg, VII., S. 21.

tissue (Glisson's capsule), which encloses the vessels, containing bile and blood, that are situated between the layers of the hepatico-duodenal ligament. A case of this kind was described by Frerichs (l. c., II., S. 370), in a man, æt. forty-six years, who was suffering from marked ascites. The portal vein was considerably stenosed, its lumen presented an angular appearance on cross-section, and the vessel was surrounded by firm connective-tissue masses. The trunk of the portal vein, in the transverse fissure of the liver, was unusually narrow, and filled with brownish red, crumbling clots, which projected into the hepatic branches, and there assumed a homogeneous, blackish red appearance. The thrombus was only adherent in spots to the wall of the vein, which retained its original smoothness. The case described by Barth[1] is exactly similar. Ziegler (l. c., S. 7) reports the case of a man who had lost a large amount of blood from a chronic duodenal ulcer. At the autopsy the ulcer was found connected with a thick layer of new-formed connective tissue, by the retraction of which the vena portæ had been entirely compressed. Within the vein was found a laminated, centrally softened thrombus, which extended far into the liver, both in the right and left portal branches. The liver presented a normal appearance, and the gall-bladder was filled with a large quantity of thick bile. Unfortunately the mutual relations of these changes to one another are not clearly defined. Frerichs (l. c., I., S. 280) also describes a case in which, in consequence of a perforating duodenal ulcer, new-formed connective tissue had formed around the portal vein, and compressed the trunk of the vessel. The vessel contained a laminated thrombus, which had become cheesy in the centre, and extended deep into the liver.

Circumscribed thrombosis may also occur occasionally in the radicles of the portal vein, in the splenic and large gastric veins, in consequence of chronic inflammatory processes of the diaphragm when the inflammation spreads to the walls of the veins in question.

Compression of the portal vein outside the liver is produced

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[1] Bull. de la soc. anat., 1851, p. 354.

much more frequently by various growths which start from the neighboring organs than by new-formed masses of connective tissue. We must specially mention cancers of the stomach, pancreas, and duodenum, of the portal and retro-peritoneal glands, and tubercular-cheesy, leukæmic, and lympho-sarcomatous tumors of the glands in the hepatico-duodenal ligament. In addition to compression, these tumors usually give rise to true pylethrombosis, and the thrombus may fill either the trunk or the large radicles of the portal vein, or both. The extent of the thrombosis is very variable in such cases. However, the lumen of the vessel is not always entirely occluded, but only partial obturation occurs, so that the blood may still continue to flow.

Special mention must finally be made of those cases which are presented to the anatomist under the appearances of hob-nailed liver and which are usually termed *adhesive pylephlebitis*. At this place, when we are discussing the etiology, we need not refer to the question whether adhesive pylephlebitis is really as frequent as Rokitansky and others believe, or whether the cases which are thus referred to actually belong to this category. At the present time no one doubts that many cases of this character have nothing in common with pylephlebitis, but are due to constitutional syphilis, irregular interstitial hepatitis and similar processes, in which the branches of the portal vein, if at all occluded, are only secondarily and accidentally affected. However, some cases of hob-nailed liver still remain in which the deformity of the organ must be attributed to the fact that a number of branches of the portal vein have been converted into solid strands of connective tissue, the retraction of which has drawn the surface of the liver inward. In these cases of true adhesive pylephlebitis, which, as a matter of course, have been preceded by coagulation of blood in the corresponding branches of the portal vein, we should endeavor to determine the exciting cause, and the manner in which the primary pylethrombosis was produced. We are almost at a complete loss in this regard, as none of the known causes of thrombosis appear applicable to these cases. This is also conceded by Frerichs, who has several times observed the process in question after long-continued intermittent fever (combined with old enlargement of the spleen),

and regards it as probable that the occlusion of the branches of the portal vein has been due, in many cases, to errant clots, originating in the splenic vein, or some other radicle of the portal vein. The subject is rendered still more involved by the fact that obliteration of the hepatic branches of the portal vein occurs without any signs of an hepatic affection, such as ascites, etc. (Frerichs).

Pathological Anatomy.

The variations in the situation and extension of the thrombus depend chiefly upon the exciting causes. At times the thrombus only involves the hepatic branches of the portal vein; at other times the trunk is also occluded, and the plug frequently extends for a variable distance into the portal radicles, and sometimes close to their origin. As a rule, the thrombus entirely occludes the lumen; peripheral, only partially occluding thrombi, are rarely observed. The distal end of old thrombi often presents a hemispherical appearance,[1] but usually it is continuous with fresh, soft clots which are gradually lost in the fluid contents of the portal radicles. The central end of the thrombus generally extends deep into the liver, so that the branches of the portal vein appeared to be occluded down to their final ramifications.

Thrombi of the portal vein do not vary appreciably in character from those of other veins. In marasmatic thrombosis, in which the mass of blood coagulates as a whole, the thrombi present a blood-red color, a soft, moist consistence, and are homogeneous, or indistinctly laminated. But when the thrombosis develops gradually, laminated white thrombi are formed, which only consist of fibrin and leucocytes. Primarily, these clots are also soft and moist. In time the thrombus becomes firmer, drier, and more brittle, the red coagula grow paler, and assume a brownish, later, a dirty, grayish yellow color. The ordinary metamorphosis of these thrombi, when sufficient time has elapsed for such a change, consists of drying, retraction, and simple necrosis, by which the plug, at least in its central portions, assumes

[1] *Vide* the drawing in Carswell, l. c.

a firm, cheesy consistence. Softening and degeneration of the centre of the thrombus into a dirty, pale gray, pasty mass also occurs, though exceptionally. True organization of the thrombus, as is found in true pylephlebitis adhesiva, is, in reality, not often observed. It has only been found in the territory of the hepatic branches, but not in the trunk and radicles of the portal vein. Moreover, we do not often observe, in the dead-house, the early stages of so-called organization of the thrombus, but only the sequences of the process; *i.e.*, we find the portal branches in question converted into firm, solid, fibrous cords, in which no trace of the vascular wall, or of the mass which had filled the lumen of the canal, can be detected.

In autopsies of individuals who have suffered from occlusion of the portal vein, we usually find the trunk of the vessel dilated, and converted into a hard strand about as thick as the thumb. The walls of the vessel are usually thickened, and sometimes appear like those of an artery. The thrombus is firmly adherent to the vascular walls. In recent cases of pylethrombosis, especially in the marasmatic form, the tunica intima is almost unchanged, or, at the most, diffusely infiltrated with blood-pigment. After long continuance of the thrombosis, on the other hand, it appears dull, opaque, of a dirty, grayish yellow color, and brittle. The external walls of the vein are thickened, succulent, and markedly congested, in consequence of the secondary inflammation by which the thrombus was produced. In very old cases, marked hyperplasia of connective tissue, fatty degeneration, calcification, and ossification may change the original character of the walls of the vein so as to render them unrecognizable.

The remaining changes in the bodies of these individuals are either entirely unconnected with the pylethrombosis or they are the sequences of the portal occlusion. The latter include the phenomena of stasis in the territory of the radicles of the portal vein, the changed circulatory relations in the abdomen, especially the dilatation of certain groups of veins as a means of compensation for the disturbances in the territory of the portal vein, and finally certain anatomical changes in the liver itself.

The phenomena of stasis are a necessary and, therefore, con-

stant result of portal occlusion. Apart from the dilatation of the abdominal veins, they include ascites, enlargement of the spleen, venous congestion of the radicles of the portal vein, especially in the gastric and intestinal mucous membrane, which often gives rise to hemorrhage, partly into the tissue of the mucous membrane, partly into the cavity of the gastro-intestinal tract. As a matter of course, the symptoms of stasis are only present when the portal blood cannot pass through any other channels. The more complete the collateral circulation, which we shall soon discuss, the more the signs of stasis of the blood step into the background or even remain entirely absent.

The character of the changes in the abdominal circulation depends upon the duration of the portal occlusion, its causes, and, in general, upon the peculiarities of the individual case. Two points must be considered in this respect, viz., the flow of blood from the radicles of the portal vein, and the compensation which the liver receives for the portal blood which is withheld.

As the blood in the portal radicles cannot pass through the liver, it must seek new paths in order to reach the heart. We have already referred to these paths; they include the anastomoses, which are normally present but slightly developed, between the territories of the portal vein and that of the inferior, to a less extent of the superior vena cava (*vide* p. 781). The passage of the blood of the portal vein through these originally capillary anastomoses, in order to reach the venæ cavæ, causes them to become enormously dilated, and they are gradually transformed into thick-walled veins, which are often as thick as a raven's quill, or even the little finger, and usually run a sinuous course.[1] All these anastomoses are not employed in every case, but the blood seeks especially this or that channel, according to the permeability of one or another portion of the portal vein. In the living subject merely the supplementary circulation through the dilated veins of the abdominal walls is visible; the remaining channels only come under our observation at the autopsy. But even the collateral circulation through the abdominal veins only develops when the impermeability is restricted

[1] *Vide* the vena parumbilicalis (the supposed umbilical vein) in the beautiful drawing in Cruveilhier. Atlas d'anat. path., livr. 16, pl. 6.

to the hepatic branches of the portal vein, while the trunk of the vessel is not occluded. In such a case the blood in the portal vein flows through the enormously dilated vena parumbilicalis (*vide* p. 782) to the umbilicus, where it empties into the broad and sinuous subcutaneous veins of the abdominal walls, and through these partly into the internal mammary and epigastric veins, but chiefly into the saphena and femoral veins. The entire complex of sinuous phlebektasiæ under the integument of the abdomen, which is perceptible to touch as well as to sight, has received from Marcus Aurelius Severinus[1] the appellation caput medusæ.

The functions of the hepatic parenchyma do not cease entirely after portal occlusion, though they are considerably interfered with or diminished. At least, the secretion of bile suffers no interruption; in certain cases, even in complete occlusion of the portal vein, it does not appear to be at all changed. We must, therefore, assume that the liver receives a substitute for the blood of the portal vein which is withheld. In many cases the hepatic artery probably furnishes the substitute, and, under such circumstances, it is sometimes found dilated. The investigations of Cohnheim and Litten, referred to above (p. 784), have enlightened us with regard to its connection with the interlobular veins and the capillary network of the acini of the liver, and thus with regard to the manner in which the blood of the hepatic artery is employed as a substitute for that of the portal vein.

The above-mentioned accessory portal veins (p. 781), especially the group which starts from the diaphragm, may serve as an additional source of blood necessary for the hepatic functions. The vena parumbilicalis, which we have mentioned as a channel for the discharge of portal blood, may, under other circumstances, serve for the passage of blood from the superficial veins to the liver, when the pylethrombosis is restricted to the roots and beginning of the trunk of the portal vein, while the hepatic branches and the sinus venæ portæ are permeable. The direction of the valves in the last-mentioned veins is an indica-

[1] De abscess. recordit. cap. IX., § 13.

tion that they are intended for the passage of blood in the direction toward the liver.

With regard to the condition of the liver in occlusion of the portal vein, it is not always easy to decide whether certain changes should be regarded as the cause or result of portal occlusion. In recent cases, in acute pylethrombosis, the liver is found anæmic, flaccid, but without any other appreciable change. After long-continued occlusion, on the other hand, the liver is more or less atrophied, the surface sometimes smooth, sometimes granular, its consistence firm, its tissue anæmic. It is generally believed that the chronic atrophy of the liver is the primary disturbance which has given rise to occlusion of the portal vein. However, others have interpreted this in the opposite sense, and believe that the chronic occlusion of the portal vein has been the starting-point of the atrophy and induration of the liver. Solowieff[1] has endeavored to base the latter view upon experiment, inasmuch as he produced occlusion of the trunk of the portal vein and its hepatic ramifications by continued thrombosis, by artificially occluding one or the other branch of the vena portæ (in dogs). It was found that, in this manner, a process was induced which corresponded to interstitial, fibrous hepatitis, and that it is therefore justifiable, under certain circumstances, to attribute indurated atrophy of the liver to occlusion of the portal vein.

The cases of (primary?) adhesive pylephlebitis (which are problematical in many respects), with organization of the thrombus and obliteration of the vessel, present the following anatomical appearances: The liver is only slightly atrophied, but of a deformed shape. Deep, furrowed retractions of the serous covering, which give to the organ a lobular appearance, are observed at various parts of the surface, especially of the right lobe. If the liver is incised in various directions, it is found that white fibrous bands pass from the bottom of the furrows toward the transverse fissure of the liver and correspond to the completely obliterated branches of the portal vein. These fibrous bands also

[1] Virch. Arch., LXII., S. 195 (1875). Also see *Klebs*, Handb. d. path. anat., I., S. 412, who refers to rusty brown pigment atrophy of the liver as a sequence of chronic occlusion of the portal vein.

impart a lobulated character to the cut section of the organ. The parenchyma of the liver sometimes appears entirely intact, sometimes it is indurated and atrophic in the neighborhood of the destroyed vessels by the hyperplasia of interlobular connective tissue. We have previously stated that the lobular syphilitic liver and other processes, which do not belong here, have often been grouped with the form just described. If we note the course of the fibrous bands within the liver we will find that they do not always, by any means, correspond to the direction pursued by the branches of the portal vein.

Pathology.

General Clinical History.

Whoever has carefully studied cases of portal obstruction will regard it as difficult to give a history of this disease, which can lay claims to general acceptance, as very material changes in the clinical history are produced by the sometimes acute, sometimes subacute, or even almost latent course of the process of occlusion, by the nature of the diseased process which has given rise to the occlusion, and by all kinds of secondary and accidental circumstances. But there is, nevertheless, in the large majority of cases, a noteworthy uniformity in the essential symptoms of the disease, so that its character is recognized without much difficulty in a concrete case.

After long duration of those diseased conditions which are known to act as exciting causes of pylethrombosis, as, for example, cirrhosis, chronic peritonitis, phthisis, and other affections which are associated with extreme marasmus and weakness of the heart, the most marked symptoms of stasis of blood, in the organs belonging to the territory of the radicles of the portal vein, develop either gradually or unexpectedly and almost suddenly. The accumulation of a large quantity of fluid in the abdominal cavity occurs with special rapidity. Within a few days the ascites attains extraordinary dimensions, and, when puncture is performed, the abdominal cavity usually refills with water within a day. The spleen increases in size at the same

time, and soon attains from twice to four times its normal dimensions. Furthermore, the subcutaneous veins of the abdominal walls appear as a plexus which has a bluish appearance through the integument. They are enormously dilated and sinuous, and extend from the umbilicus downward to the inguinal region and upward to the lower portion of the anterior wall of the thorax and to the axillæ. In the meantime diarrhœa of a sero-mucous character has appeared, and the thin passages are often mixed with very considerable quantities of blood. In addition, emesis, often of bloody masses, frequently occurs. The secretion of the kidneys is very scanty, and the urine is correspondingly concentrated, but generally free from albumen. This condition leads to rapid deterioration of the entire organism. Œdema of the lower extremities occurs, and the fatal termination develops more or less rapidly after increasing exhaustion.

The variations from the usually observed symptomatology described above depend upon the completeness or incompleteness of the portal obstruction, whether the pylethrombosis spreads rapidly or slowly; furthermore, which portions of the vessel are occluded, and which permeable, but especially do they depend upon the completeness of the collateral circulation, which has developed in favor of the blood that is stagnating in the radicles of the portal vein.

Symptoms.

If we consider the symptoms of portal occlusion individually, we must first call attention to the absence of local symptoms in this disease. The occluded portal vein cannot be perceived directly, either by sensation or in any other manner. At the most, pain is present when the wall of the vein experiences a considerable degree of inflammatory irritation from the thrombus. The situation of the pain is variable; it is not necessarily located in the trunk of the portal vein, but may also be situated in the thrombosed radicle of the vessel, which is in a condition of inflammatory irritation.

The foreground is occupied by those symptoms which are the mechanical results of the stasis of blood produced by the portal

occlusion, viz., ascites, enlargement of the spleen, diarrhœa, and admixture of blood with the passages and vomited matters. The formation of the venous plexus in the abdominal walls is almost co-ordinate with the symptoms just mentioned.

If ascitis is not produced by the primary affection which has given rise to the pylethrombosis, it will develop soon after the occlusion of the portal vein, and attains the highest grades with surprising rapidity. Its renewal occurs with equal certainty and rapidity after the fluid has been removed from the abdominal cavity by puncture. Although the ascites must be regarded as a necessary sequence of the portal occlusion, it has been found absent in a few cases of total pylethrombosis, involving the trunk and branches of the vein, but only because compensatory relief of the stasis occurred by copious hemorrhages from the stomach and intestines, or by the prompt and sufficient development of the collateral circulation, especially by means of the dilated veins in the abdominal walls.

The same remarks hold good with reference to the enlargement of the spleen. It occurs from the same mechanical causes, with equal rapidity, and, on the whole, with as great certainty as the ascites. But it is also absent sometimes in pylethrombosis, partly because relief of the stasis occurs by hæmatemesis and bloody stools, partly because the spleen has been previously degenerated, and is therefore not susceptible of further enlargement.

The dilatation of the subcutaneous abdominal veins is not a constant symptom of portal occlusion, but is only observed in about half the cases. This is readily explained as the fact that the blood secures collateral channels for its discharge in the direction toward the umbilicus and into the veins of the abdominal walls must be rather regarded as a lucky chance than as a necessary consequence of the conditions in question. The phlebektasis of the abdominal walls is usually most marked when, in addition to the portal vein, the inferior vena cava is also occluded, as the veins of the abdominal walls, together with the vena azygos, constitute the only channel by which the blood is conveyed from the lower half of the body to the superior vena cava. However, the "Medusa head" is not symptomatic alone of pyle-

thrombosis. It is also observed in ascites which follows heart disease, pressure of tumors upon the inferior vena cava, etc. In the latter cases dilatation of the veins of the thigh is also usually present. It must not be forgotten that in severe ascites the abdominal veins are more distinctly visible, even though they are not dilated, on account of the stretching of the abdominal walls and the disappearance of adipose tissue.

Diarrhœa is the most constant symptom on the part of the intestinal tract, and is analogous to the ascites in its mode of development; both are the result of increased transudation of serum from the stagnant blood of the capillaries. Diarrhœa is exceptionally absent when the evacuation of the radicles of the portal vein is effected by a well-developed collateral circulation. In about one-third of the cases the watery passages are mixed with a considerable amount of blood, and sometimes appear to be composed almost entirely of pure blood. Hæmatemesis also occurs frequently in combination with the bloody passages. In some patients these hemorrhages constitute the first and almost only symptom of pylethrombosis, as the individual dies before the ascites and remaining symptoms could develop.

The dyspeptic symptoms which are usually present are of minor importance as characteristics of pylethrombosis. But mention should be made of the observation first made by Stokes, that some patients suffering from chronic portal occlusion show a striking increase in their nutritive requirements. An explanation has been furnished by the statement that, under such circumstances, the formation of blood must be disturbed, because the peculiarly constituted blood of the intestinal canal is not sent to the liver for further transformation, while the latter organ receives blood which is less adapted to it, viz., that from the arteries and veins of the trunk.

From causes which are readily understood, the secretion of urine is diminished, very concentrated, of a bright yellow color, free from albumen in uncomplicated cases, and deposits a heavy sediment of urates.

The liver presents a variable appearance. It is sometimes of normal dimensions, but usually reduced in size, though exceptionally enlarged. These variations depend in great part upon the

primary hepatic affection to which the pylethrombosis has been superadded. The liver is usually atrophied, because cirrhosis so frequently gives rise to pylethrombosis. In other cases the atrophy of the organ must be regarded as a sequence of chronic portal occlusion. It is found enlarged in those cases in which cancerous growths within it have acted as the exciting cause of the pylethrombosis. It is a remarkable fact that the secretion of bile is not appreciably disturbed in portal occlusion. The liver draws its material, as we have seen, from the hepatic artery and the accessory portal veins. Icterus is observed in only a small proportion of cases. When it does occur, it stands in no direct causal relation to the pylethrombosis.

General symptoms, which affect the entire organism, do not belong to portal occlusion, and fever, rise of temperature, etc., do not occur. However, a condition of general marasmus, emaciation, and loss of energy rapidly develops, and œdema of the lower extremities appears (later than the ascites) and continues until death.

Diagnosis.

The diagnosis of portal occlusion depends upon the demonstration of ascites, enlargement of the spleen, diarrhœa, bloody stools, hæmatemesis, and upon the presence of dilatation of the abdominal veins. If these symptoms of stasis are combined, there can be no doubt that the portal vein is impermeable. On the other hand, the diagnosis may be very difficult when ascites or several of the symptoms mentioned above are absent. If ascites is present in such doubtful cases, its rapid return after puncture is evidence of the presence of pylethrombosis.

Strictly speaking, the above-mentioned symptoms of stasis merely indicate portal occlusion, but they do not decide whether the impermeability is due to pylethrombosis or to some other condition. In fact, cirrhosis of the liver without portal thrombosis may present the same symptoms, and the clinical history is sometimes so much alike in the two affections that they are readily mistaken one for another, especially when the patient is seen for the first time. The previous history usually furnishes

useful data for the differential diagnosis of these diseases. The most important factor, however, which permits us to assume pylethrombosis is the extraordinarily rapid development of the symptoms of stasis, and sometimes, also, the presence of certain abdominal affections which we know, from experience, may act as pathogenetic factors of pylethrombosis.

Course, Duration, Terminations, Prognosis.

Pylethrombosis may run either an acute or chronic course. This depends, in the main, upon the etiological relations of the individual case. The course is acute when the thrombosis is due to general marasmus, heart failure, cancer of the liver, etc. It is chronic in many cases in which the pylethrombosis supervenes upon cirrhosis of the liver, and in idiopathic cases of adhesive pylephlebitis (in the true sense). However, the duration and course of portal occlusion depend, in great part, upon the completeness of the collateral circulation, by which the effects of the stasis are counteracted.

In the majority of cases the duration is short, from a few days to several weeks. But examples are also known in which the condition has lasted for months, and some even in which the compensatory collateral circulation was so complete that the pylethrombosis existed for years as a stationary condition without any special distress to the patient. To this category probably belongs the case represented by Cruveilhier (l. c.), and which I can only interpret as chronic adhesive pylephlebitis.

Pylethrombosis almost always terminates fatally, and a radical anatomical cure is scarcely conceivable. Exceptionally, however, such a complete compensation of the symptoms of stasis may occur by the opening of new channels for the escape of the blood in the territory of the portal radicles, that we may speak of a termination in recovery. Such compensation is, however, only conceivable in those cases in which the parenchyma of the liver is not appreciably changed.

In general, therefore, the prognosis of pylethrombosis must be considered unfavorable, and the fatal termination regarded as not far distant. There are very rare exceptions to this rule.

Treatment.

Therapeutics is powerless against occlusion of the portal vein. It is restricted to ameliorating the annoying and dangerous symptoms which are due to the stasis of blood as much as possible. The diarrhœa and hemorrhages from the stomach and intestines may be combated by various astringents, viz.: tannic acid, rhatany, liq. ferri sesquichlorat., etc., but good results will be rarely obtained. The ascites, which rapidly attains a dangerous height, can only be temporarily relieved by puncture. But it lies in the nature of the disease under consideration that the transudation almost immediately regains its former dimensions. As the inanition of the body and marasmus are furthered by the removal of the fluid, we must wait as long as possible before repeating the puncture, and the danger of suffocation will alone justify the repeated performance of this operation, whose good effects are only experienced, at the most, for a few hours. The ordinary remedies, such as diuretics and drastics, should not be employed in ascites due to portal occlusion. The diuretics are generally useless, especially in marasmatic thrombosis, because the pressure of blood in the vessels of the kidney cannot be increased on account of the weakness of the heart, and drastics would increase to a still higher grade than certain diuretics the irritated condition of the intestinal mucous membrane and thus intensify the marasmus. The only rational indication is to combat, as much as possible, the threatening marasmus, the loss of energy, and especially the weakness of the heart. If we succeed in strengthening the heart's action and stimulating the circulation, we would not alone diminish a pathogenetic factor of the pylethrombosis, but we would also aid the compensation of the portal stasis by the development of vigorous collateral circulation. This indication is met by the administration of concentrated but easily digested food, good strong wine, and preparations of iron and quinine.

Purulent Inflammation of the Portal Vein.

(Pylephlebitis suppurativa, ulcerosa.)

Sasse, Dissert. de vasorum sanguiferor. inflammatione. Halæ, 1797.—*Bouillaud*, Arch. gén. de méd. II., p. 198. 1825.—*Reynaud*, Journ. hebdom. 1829, 43.—*Dance* and *Arnott*, Ueber Venenentzuendung u. deren Folgen, German by *Himly*. Jena, 1830 (contains the admirable treatise by *Dance*, De la phlébite utérine, etc., from the Arch. gén. de méd., Dec., 1828; Janv. et Fev., 1829).—*Baczynski*, De venæ portarum inflammatione. Diss. Turici, 1838.—*Mohr*, Berl. med. Centralztg. IX. Jahrg., No. 29.—*Käther*, De venæ portarum inflammatione. Diss. Berlin, 1840.—*Sander*, De venæ port. inflamm. Diss. Berlin, 1841.—*Schoenlein's* Klin. Vorträge. Edited by Gueterbock. 2 Aufl. Berlin, 1842. S. 275–301.—*Lambron*, Observ. de l'inflammation des veines du foie. Arch. gén. de méd. Juin, 1842.—*Puchelt*, Das Venensystem in seinen krankhaften Verhältnissen. 2 Aufl. Leipzig, 1844.—*Budd*, Diseases of the Liver. German by *Henoch*. Berlin, 1846. S. 160.—*Schuh*, Ztschr. d. Ges. d. Wien. Aerzte, Feb., 1846.—*Waller*, ibid. Sept. and Oct., 1846.—*Oppolzer*, Bemerkungen z. Path. d. Leberentzünd. Prager Vierteljahrschr. 1847. 13 Bd., S. 114.—*Fauconneau-Dufresne*, Mém. sur l'inflammation du système veineux abdominal. Gaz. méd. de Paris. VII., p. 729. 1849.—*Raikem*, Edin. Journ. April, 1850.—*Reuter*, Ueber Entzünd. d. Pfortader. Diss. Erlangen, 1851.—*Leudet*. Arch. gén. de méd. 1852.—*Buhl*, Pylephlebitis nach Perfor. d. Wurmfortsatzes, etc. Ztschr. f. rat. Med. N. F. IV. 1854, S. 348.—*Henoch*, Klinik d. Unterleibskrankhtn. I. Bd., 2 Aufl. Berl., 1855, S. 202.—*Langwagen*, De venæ port. inflamm. s. pylephlebitide. Diss. Leipzig, 1855.—*Bamberger*, Krankh. d. chylopoët. Systems. Virch. Handb. d. Path. u. Ther. VI. Bd., 1 Abth. Erlangen, 1855, S. 637.—*Wunderlich*, Handb. d. Path. u. Ther. III., 3, S. 322. Stuttgart, 1856.—*Bristowe*, Pylephlebitis after Chronic Gastric Ulcer. Path. Trans. IX., p. 279, 1858. Gangrenous Pylephlebitis caused by Gall-Stones. Ibid., p. 285.—*Frerichs*, Klinik d. Leberkrankh. II. Braunschw., 1861, S. 385.—*Buhl*, Fall von Ulcerativer Pylephlebitis. Virch. Arch. Bd. 31, S. 480, 1861.—*Von Jan*, Ueber Pfortaderentzündung. Diss. Erlangen, 1866.—*Moers*, Pylephlebitis nach Verschwärung des Wurmfortsatzes. Deutsch. Arch. f. klin. Med. IV. 1868, S. 251.—*Fraentzel*, Ein Fall von Pylephlebitis nebst diagnostischen Bemerkungen. Berl. klin. Wschr. 1869, S. 313.—*Aufrecht*, Entzündung d. Proc. vermiform. Pylephlebitis. Ibid., S. 308.—*Chvostek*, Thrombose d. Pfortader mit Eiterähnlichem Zerfall d. Gerinnsel (*vide* Virch. u. Hirsch. Jahresb. f. 1869. II.).—*Schueppel*, Ueb. Peripylephlebitis syphilitica b. Neugeborenen. Wagner's Arch. d. Heilk. XI. 1870, S. 74.—*Payne*, Two Cases of Suppuration in the Appendix Vermiform. Path. Trans. 1871.—*Legg*, Purulent Portal Thrombosis from Cancerous Ulcers of the Stomach.

Path. Trans. Vol. XXV. 1874, p. 123.—*Quénu*, Pylephlebitis Suppurativa nach Gallensteinen. Gaz. méd. de Paris. No. 51, 52, 1878.—*Thomas Le Dieu*, De la pyléphlébite suppurative. Paris, 1879.

The conjecture entertained by Schoenlein that suppurative pylephlebitis would prove, in time, a not very rare disease, has since received complete demonstration. On the other hand, I cannot accept the view entertained by many others, that the suppurative form of inflammation of the portal vein is much rarer than the adhesive, especially when a distinction is made, as there should, between simple thrombosis and adhesive phlebitis. On the contrary, true adhesive phlebitis appears to occur very rarely in comparison with the suppurative form.

Purulent inflammation of the portal vein occurs at every period of life from birth to old age. It is generally a secondary process which supervenes upon suppurative conditions and ulcerations in various abdominal organs. It occurs only exceptionally as a primary idiopathic disease. It never extends over the entire system of the portal vein, but, in addition to the trunk of the portal vein, a few radicles and all or some of the hepatic branches—sometimes the latter alone—are affected.[1]

The abnormal changes in suppurative pylephlebitis pursue the following course: an inflammatory process in the vicinity of the portal vein spreads to the latter, produces a condition of purulent infiltration in the wall at this place, and causes coagulation of the blood in those portions of the vein which were first affected. The thrombus undergoes purulent softening, the lumen of the vessel appears filled with pus, or with a greasy, purulent, ichorous fluid. The inner surface of the vessel may even become ulcerated. When the process just described has occurred in the trunk of the portal vein, the thrombus spreads to the hepatic branches, and, perhaps, for some distance backward into the radicles. The secondary thrombus then undergoes the same purulent changes as the primary. In the territory of the secondary thrombus the hitherto intact vessel also undergoes inflam-

[1] A local purulent phlebitis has also been observed, restricted to a few places in one or another portal radicle, without any subsequent inflammation of the trunk of the portal vein, or of its hepatic branches. Compare *Virchow*, Ges. Abhandl., S. 569, 572, and in other places.

mation, and the peculiar (often septic) constitution of the thrombus causes the development of an intense inflammation of the wall of the vein (proceeding to suppuration) which may even spread to the adjacent parenchyma of the liver (purulent hepatitis). When, on the other hand—as usually occurs—the disease starts in a radicle of the portal vein, the course of the changes is in general the same as that already described, but the following points must also be taken into consideration. As a rule, the preparatory or secondary thrombosis spreads uninterruptedly, from the original site of the disease, along the affected vessel into the trunk, and then further into the hepatic branches; puriform softening of the thrombus develops throughout this whole extent, with accumulation of pus in the vein, purulent infiltration, and, finally, ulcerative degeneration of the wall of the vein. Exceptionally, however, the primary thrombus is confined to its original site, and no continuation of the thrombus occurs in the direction of the liver. Pieces of the softened primary thrombus may then break off, and be carried as emboli into the hepatic branches of the portal vein. Here they are arrested, cause coagulation of blood until the affected vessel is entirely occluded, the thrombus grows backward, gradually fills the larger branches, also undergoes purulent metamorphosis, and puts the walls of the portal vessels in a condition of purulent infiltration and ulcerative destruction.

Etiology.

Purulent inflammation of the portal vein rarely develops as the result of a direct lesion of the vascular walls, and it then constitutes a primary, traumatic pylephlebitis. The best known example of this kind is the often-quoted observation of Lambron:[1]

In an old man a fish-bone about three centimetres long, and as thick as a large pin, was found in the head of the pancreas. It had perforated the anterior wall of the superior mesenteric vein, extended for some distance into the lumen of the vessel, and the point was imbedded in the opposite wall of the vein. The bone appeared to have perforated the posterior wall of the stomach near the pylorus,

[1] Arch. gén. de méd., 1842, p. 129.

and to have entered the vein through the head of the pancreas. As a matter of course, purulent inflammation of the vein developed at the corresponding point, and afterward spread to the portal vein and its branches.

The following case, reported by von Jan,[1] is very similar to the previous one in regard to its manner of development.

A man, æt. fifty years, who had been insane for a long time, swallowed various foreign bodies with suicidal intent. At the autopsy, a piece of stout wire, eleven centimetres long, was found to have penetrated the upper posterior wall of the duodenum, near the pylorus. The upper end of the wire lay in the cavity of the duodenum; the other end, which is directed to the left and downward, is sharp, and appears free in the abdominal cavity after having passed through the root of the mesentery. Immediately above the canal, in which the wire is situated, is found the superior mesenteric vein as a firm cord, filled with a loose thrombus. The portal inflammation had been due to this.

With traumatic pylephlebitides are ranged, in etiological relation, those cases in which the portal inflammation starts from the umbilicus; this is the pylephlebitis of the new-born. In individual cases it may be interpreted as a continuous, simple traumatic inflammation of the vein. In other cases we have to deal less with a simple inflammatory affection than with pylephlebitis due to septic infection.

A case recently observed by me may be interpreted in this manner. A child, two weeks old, was taken sick with severe fever, and died one week afterward. The umbilicus had always presented a normal appearance. At the autopsy, also, the lower part of the umbilical vein appeared entirely healthy, but the upper third, the trunk of the portal vein, and the branches going to the right lobe of the liver were dilated, and filled with thick, foul-smelling pus. An interpretation of the phlebitis as a simple traumatic one, is contradicted by the fact that the umbilicus appeared at no time to be the site of perceptible inflammation. The assumption of a septic pylephlebitis, however, appears entirely plausible. The infectious matter (bacteria) may have entered the umbilicus in extremely small quantities, and have been carried farther without giving rise, in the latter, to any perceptible affection. Inflammation of the vein only occurred after the infectious matter had been correspondingly increased, and had thus acquired phlogogenic power.

By far the larger number of cases of suppurative pylephlebitis may be attributed to the presence of an inflammatory or ul-

[1] Ueber Pfortaderentzündung, Diss., Erlangen, 1866, p. 29 ff.

cerative focus within those organs from which the radicles of the portal vein start. Such foci first produce a phlebitis, which is confined to a few veins, and this then spreads continuously along the course of the vessel to the trunk of the portal vein and its hepatic branches.

Sometimes fragments of thrombi from the primarily affected vein are carried as emboli into the hepatic branches of the vena porta, and thus produce pylephlebitis discontinuously. In both cases the inflammatory irritant affecting the walls of the vein must be sufficiently strong to give rise to suppuration. This occurs so much the more readily because the inflammatory products surrounding the vein and the thrombi, and other contents within it, possess, as a rule, infectious, septic qualities, corresponding to the character of the original diseased process.

The most common case included in this category is that in which the pylephlebitis is due to suppuration and ulceration in the vicinity of the cæcum and its vermiform appendix. These very cases, which supervene upon perityphlitis, may serve as a type for the pathogenesis of suppurative pylephlebitis. A large number of them have been described in a former period by Mohr, Waller, Buhl, and lately by Moers, von Jan, Axel Key, Payne, Fraentzel, Aufrecht, and others. It is of slight importance whether the perityphlitic suppuration spreads over a large surface, whether it is combined with ichorous and gangrenous degeneration of tissue, with severe peritonitis, etc., or whether there has been a slow perforation of the vermiform appendix by firm fæcal masses, etc. The necessary link is the implication of the mesenteric veins in the inflammatory process. One vein or another, in the territory of the ichorous or purulent process, is affected by the inflammation, becomes filled with blood-clots, which rapidly undergo purulent softening, while the wall of the vein and its connective-tissue sheath appear infiltrated with pus. The phlebitis then spreads uninterruptedly along the affected vein until it reaches the trunk of the portal vein and its hepatic branches, or the transition from the primary focus to the hepatic branches occurs by embolism, in which event a healthy portion of vein is inserted between the affected parts of the vessel. The latter is observed more rarely. That no period of life is spared

by purulent pylephlebitis depends chiefly upon the fact that perforation of the vermiform appendix and perityphlitic processes occur at every age, even in children and young people. The pylephlebitides developing in this manner always present a septic character. The entire series of abnormal changes may be interpreted as thrombo-embolic pyæmia, confined to the territory of the portal vein, as metastatic abscesses are only exceptionally found in other organs (lungs, brain, kidneys).

Purulent pylephlebitis develops much more rarely from a suppurative process of the stomach or some other portion of the intestinal canal than from the cæcum and vermiform appendix. Bristowe[1] found pylephlebitis originate from inflammation of the veins in the vicinity of a chronic gastric ulcer, which had spread to the pancreas. A similar observation was made by Bamberger. Marotte[2] saw pylephlebitis develop in consequence of ulcers of the large intestines. (Perhaps the hepatic abscesses occurring in dysentery have a similar mode of origin, inasmuch as they are preceded by phlebitis of the intestinal veins and embolism of the hepatic branches of the portal vein, but, on account of the small size of the emboli, extensive pylephlebitis does not occur.) Purulent pylephlebitis has also been found to start in the rectum, and always through the connecting link of hemorrhoidal phlebitis. A rectal fistula (Borie), a wound of the rectum by the end of a syringe (Leudet), removal of hemorrhoids by operation (Bamberger and others) are the starting-point, in such cases, for the long series of abnormal phenomena which reach their culmination in pylephlebitis.

Furthermore, suppurative pylephlebitis has been several times found to depend upon a purulent or ichorous focus in the spleen. An abscess or gangrenous spot in the spleen spreads to the splenic vein, and the inflammation of the latter is propagated to the trunk of the portal vein and its hepatic branches. Observations of this kind are reported by Frerichs (l. c., II., S. 394) and Law.[3]

Next follow those cases of pylephlebitis in which a purulent deposit is found between the layers of the mesentery, and the

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[1] Path. Trans., Vol. IX., p. 279. [2] Revue méd.-chir., Mars, 1850.
[3] Dublin Quart. Journ., Feb., 1851, p. 238.

neighboring veins are involved in the inflammation, and filled with pus and degenerated thrombus masses (Leudet[1]). The focus in the mesentery is usually due to disease of the lymphatic glands, and may either be interpreted as a simple abscess of the gland or as a cheesy, degenerated, and softened lymphatic gland tumor.

The starting-point of suppurative pylephlebitis is sometimes found in diseased conditions of the liver, the biliary passages, or in Glisson's capsule and the hepatico-duodenal ligament. In these cases the radicles of the portal vein are normal, the inflammation involves, from the beginning, the trunk or the hepatic branches. At times, indeed, the trunk is entirely unaffected, and only a few hepatic branches are involved in the inflammation.

It has been found, on several occasions, that the inflammation and ulceration of the large bile-ducts, due to gall-stones, have spread to the adjacent trunk, or to a large branch of the portal vein, and thus produced true pylephlebitis. Cases of this character are reported by Dance (1828), Bristowe, Budd, Leudet, Lebert, Quénu, and others. It is extremely rare, however, that an hepatic abscess spreads to adjacent branches of the portal vein, or that pylephlebitis occurs in the neighborhood of echinococcus sacs as the result of the rupture of the latter into the vessel in question. Leudet observed a case of this kind.

The case in which Schoenlein[2] first made the diagnosis of suppurative inflammation of the portal vein, at the bedside, belongs to that category in which the pathogenetic factor of the pylephlebitis is situated in the hepatico-duodenal ligament and Glisson's capsule. In the patient in question a large, abscess-like space, which appeared to have been the residuum of an encapsulated peritoneal exudation, was found in communication with the trunk of the portal vein. The latter, together with its hepatic branches, also contained pus and thrombi which had undergone degeneration. In the observation communicated by Langwagen

[1] Arch. gén. de méd., 1853, t. I., p. 145.

[2] Vide his Clinical Lectures, edited by Gueterbock, 2d ed., p. 275 et seq., and the treatises of Sander, Kaether, and especially Messow, which are quoted at the beginning of this chapter.

an abscess in Glisson's capsule, as large as an apple, is also mentioned as the cause of pylephlebitis.

In an autopsy upon a man, æt. fifty-eight years, who had suffered from chronic tuberculosis of the lungs, intestines, etc., I observed the following appearances:[1] a gangrenous cavity, as large as a hen's egg, which was poorly defined toward the peritoneum by false membranes, lay in front of the transverse fissure of the liver. This cavity was caused by the suppuration of a cheesy lymphatic gland, a large number of which could still be found in the neighborhood of the portal vein and bile-duct. The gangrenous cavity had perforated, 1, into the duodenum, midway between the pylorus and porus biliaris, 2, into the hepatic duct, and 3, into the trunk of the portal vein, immediately before its bifurcation. There was no trace of a hemorrhage, although the opening into the trunk of the portal vein was as large as a pea. The walls of the portal vein had been superimposed upon one another in the neighborhood of this opening, and were loosely adherent to one another by a thin layer of fibrin, over an extent of one centimetre above and below. The lower part of the trunk of the portal vein and its branches were collapsed, and almost entirely empty. The majority of the hepatic branches were empty, some were filled with a blackish, gangrenous pulp, which appeared to have come from the cavity in front of the liver. Several round-worms had passed from the duodenum, through the gangrenous spot, into the hepatic bile-duct, and even into the branches of the portal vein. A round-worm of moderate size was enclosed in the right branch of the portal vein, two lay in the bile-ducts of the liver, and a fourth had begun to travel thither. The patient had had slight jaundice for a few days, the passages were almost entirely discolored. During the last few days before death several severe chills were observed, at irregular intervals, with marked increase of temperature (to 105.8° F.), which rapidly subsided.

Finally, we find in the literature several cases of suppurative pylephlebitis in which none of the previously mentioned pathogenetic factors can be discovered, and in which, therefore, the development of the disease is more or less shrouded in darkness (Balling, Reuter, Fronmüller,[2] and others). It is better to admit this deficiency than to regard exposure, abuse of liquor and similar poisons as the causes of the disease, as we are unable to explain any relation between the causes just mentioned and pylephlebitis.

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[1] Compare the article by Goeller, in the Deutsch. med. Wschr., 1879, 38 and 39.

[2] *Vide Betz's* Memorabilien, 23 Jahrg. (1878), S. 193.

Pathological Anatomy.

As we have previously become acquainted with the course of the diseased process and the sequence of the phenomena which make their appearance, as well as the abnormal changes of the abdominal organs which give rise to pylephlebitis, it only remains for us to give an anatomo-pathological description of completely developed suppurative pylephlebitis.

The diseased portions of the portal vein appear as rigid cords, the vessel is markedly thickened. Its connective-tissue sheath is of a red color, strongly injected, strewn with small extravasations, or infiltrated with pus to a variable extent. The wall of the dissected vein also appears reddened (of a flesh color) and thickened, when seen from the outside, or it is of a dirty, pale yellowish gray color and infiltrated with pus. The affected vein gapes upon a cut section. If it is opened along its length, the tunica intima appears discolored, grayish yellow, opaque, and dull, when the purulent or gangrenous contents have been removed. It often feels like velvet, and has undergone softening and ulcerative destruction. The ulceration of the venous walls (which begins within) has sometimes advanced so far in individual places, that no trace of the vessel is left, and we find, in its stead, an irregular gangrenous cavity. The diseased portions of the portal vein are separated from the healthy parts, which still carry fluid blood, by a firm, completely occluding thrombus which is firmly adherent to the tunica intima. This thrombus is sometimes very short and flat, and the collapsed venous walls appear to be almost adherent to one another.

With regard to the liver, the hepatic branches of the portal vein, either entirely or in part, are filled with pus, and in general present the above-mentioned appearances, while the hepatic tissue shows no appreciable change or, in addition to the portal branches filled with pus, there are a number of round, pus-holding cavities or abscesses. At times, only a few larger foci, about the size of an apple, are scattered throughout the territory of the affected portal branches, or there may be a large number of smaller ones, from the size of a pea to that of a cherry. These

abscesses are not sharply defined, but their walls consist of hepatic tissue, which is infiltrated with pus, and in a condition of softening and ulcerative degeneration. Their inner surface is therefore irregular, papillated, and discolored. Their cavities sometimes appear closed, but a communication can usually be demonstrated between them and an adjacent portal vein, which has been destroyed by ulceration and suppuration. The hepatic tissue situated between the gangrenous abscesses is usually soft, flaccid, anæmic, and of a greenish color.

The other anatomical changes in suppurative pylephlebitis refer to the diseases underlying the former process and to the peritonitis which, under certain circumstances, has been produced by the primary affection. The peritonitis sometimes occurs with purulent, sometimes with a more serous exudation, which is rich in flakes of fibrin. It may, however, be also absent or be restricted to the primary site of disease. The other abdominal organs show no constant and characteristic changes.

The pylephlebitis, or the pyæmia connected with it, include also the metastatic and gangrenous deposits which are sometimes found, in this disease, in the lungs, brain, kidneys, spleen, and in individual joints. Anatomically and genetically they are exactly like the metastases of ordinary thrombo-embolic pyæmia.

A long time ago I described, under the term peripylephlebitis syphilitica, a peculiar disease of the portal vein and liver, which I had found in very young, syphilitic children, who had died in the first weeks of life. The liver of these children was slightly enlarged, of a brownish green color, and very flaccid. Firm cords as thick as the little finger could be felt through the flaccid parenchyma, and these corresponded to the larger branches of the portal vein. Upon section through a cord of this kind, it is found that the lumen of the vessel is extremely narrow, has almost disappeared, and the bile-duct and branch of the hepatic artery are also enclosed in the fibrous cord and correspondingly stenosed. The entire change depends essentially upon an hypertrophy of Glisson's capsule, but the fibrous tissue is densely infiltrated with a large number of small round cells and with cheesy detritus of cells, by means of which the affected parts assume the appearance of a cheesy gumma. The affection just described involved the chief branches of the portal vein, either of both or only of one lobe, and did not extend backward beyond the sinus venæ portæ. At this situation, near the trunk of the

portal vein, the thickening of Glisson's capsule ceased quite suddenly. The umbilical vein was found entirely intact in all cases.

It is noteworthy, from a clinical point of view, that the affected children presented intense jaundice with complete discoloration of fæces, severe intestinal meteorism, accumulatiom of a serous fluid (with profuse fibrinous flakes) in the abdominal cavity, an enormous enlargement of the spleen, and profuse intestinal hemorrhages. The cases described assume a peculiar position from an anatomical and etiological standpoint. They cannot be directly classed either with pylethrombosis or with purulent pylephlebitis.

Pathology.

General Clinical History.

Other things being equal, the clinical history of suppurative pylephlebitis appears most distinctly in those cases in which the symptoms are separable from those of the diseased process which has gone before. When a perityphlitis forms the starting-point of the affection, its symptoms aid in completing and rounding off the clinical history of pylephlebitis. The prodromata of the latter present the greatest variety, according to the nature of the process which is the starting-point for the development of the portal affection: they correspond to the complex of symptoms of perityphlitis, chronic peritonitis, cholelithiasis, ulcerations of the stomach and rectum, abscesses of the spleen, etc. Equally variable is the duration of the prodromal symptoms. In rarer cases the disease begins with the symptoms of pylephlebitis itself and, in such cases, the underlying affection which has given rise to the portal disease has, for some reason, remained unnoticed, as, for instance, in certain cases of pylephlebitis of the new-born, latent ulceration of the vermiform appendix, etc.

The beginning of the inflammation of the portal vein is marked by pains in the region of the abdomen. The situation of the pain depends chiefly upon the parts of the portal vein which are first affected by the inflammation. It may therefore be located in the epigastrium, the right or left hypochondrium, the ileo-cæcal region, etc. The abdomen is somewhat distended and tense. A certain amount of nausea, followed by vomiting, may appear on the first day, but these symptoms usually develop

somewhat later, and remain constant during the entire course of the disease. A usually very severe chill soon follows the development of pain, or even precedes it by a short period. The chill is almost always followed by a well-developed hot and sweating stage, so that we may be led to regard it as a true attack of intermittent fever. This paroxysm is followed by a continued fever, which is interrupted by fresh chills of varying intensity. The latter follow no distinct type; the intervals between two attacks are of variable duration. A chill occurs almost daily, and sometimes more than one. When the pylephlebitis, as usually happens, assumes a septic character, the attacks become more violent, the patient appears very excited, exhausted, and peculiarly depressed, and on the whole is seriously prostrated. The features undergo a striking change, the eyes lie deeply in their sockets, the cheeks present a mottled red, the skin assumes a faint icteric color, the breathing is short and rapid, the pulse very frequent and small, the appetite lost, the tongue dry and covered, at a later period, with a thick, fuliginous coating. Swelling of the liver and spleen occur soon after the first chill, and both organs appear sensitive to pressure. Marked icterus develops; the skin appears of a citron yellow to yellowish green color. The scantily secreted urine is colored dark, but the passages from the bowels retain their biliary color. Diarrhœa usually exists, but sometimes the bowels are constipated. Within a few days the patient emaciates considerably, and the prostration attains the greatest severity. In addition, symptoms sometimes develop which indicate that metastatic deposits of pus have formed in the lungs, joints, etc. Toward the end a somnolent condition develops, which is interrupted by delirium and sometimes by convulsions. The chills have now ceased, the skin is covered by a cold, clammy sweat, and has a deep yellow color. The pulse is feeble and irregular, the secretion of urine ceases, involuntary evacuation of urine occurs, and the patient dies.

The entire series of symptoms is sometimes observed within a period of one or two weeks, or it may last from four to six weeks when the purulent pylephlebitis does not present a septic, but rather a simple inflammatory character. During the more protracted course the symptoms of diffuse peritonitis sometimes

become more prominent, although they do not reach a dangerous height. More danger is to be expected from the hectic condition of the patient—the emaciation, loss of power, profuse diarrhœa, continuous fever, with nocturnal exacerbations, and intercurrent chills, œdema of the lower limbs. After the lapse of several weeks the emaciation of the patient has reached its highest grade; he sinks into delirium and coma, which are followed by death.

Symptoms.

The first symptom, pain, by which beginning pylephlebitis is characterized, is never absent. It is a spontaneous pain, which increases on deep pressure with the tips of the finger, and gradually grows more distinct with the spread of the disease. It is usually situated in the epigastrium (the trunk of the portal vein) and in the right hypochondrium (corresponding to the hepatic branches). It only starts from the left hypochondrium (the spleen) in exceptional instances, when the phlebitis begins in the splenic vein, but more frequently in the ileo-cæcal region. This pain does not appear to possess any definite character, not even the burning quality referred to by earlier observers. It is usually attributed to the inflammatory irritation of the wall of the vein, but it must not be forgotten that the underlying affection may also be attended with pain, which is due to local inflammation of the diaphragm. The pain which, during the course of pylephlebitis, spreads over the entire abdomen, is undoubtedly due to diffuse peritonitis. Moreover, the hepatic region is always painful in purulent inflammation of the portal vein. But this symptom has no great importance in the disease under consideration, although it serves to aid the diagnosis of pylephlebitis.

With regard to the condition of the liver, it presents an increased size, which remains within moderate limits in three-fourths of all the cases. The enlargement of the organ is chiefly due to the formation of abscesses within it; the more numerous and larger they are, the greater will be the size of the liver. But if the collection of pus is confined to the lumen of the

branches of the portal vein, no cause can be found for any noticeable enlargement of the liver. The hepatic region is always painful in purulent pylephlebitis, but this symptom possesses only a subordinate diagnostic importance.

The spleen is also enlarged in the majority of cases, and this is due to various circumstances. It may be produced by mechanical means, by stasis of blood, when the splenic vein is also implicated in the phlebitis or thrombosis.

A rapidly developing enlargement of the spleen (sometimes combined with pains in the left side) may be explained in this manner. In other cases the cause of the splenic enlargement is due to the septic infection of the blood, which is so generally present in suppurative pylephlebitis.

On the other hand, the spleen may remain small, despite the occlusion of the splenic and portal veins and the septic infection of the blood, because fibrous thickening of its capsule or degeneration of the parenchyma renders the enlargement of the organ impossible. Perhaps the splenic hypertrophy also remains absent occasionally on account of profuse compensatory hemorrhages from the stomach and intestines; but this is not very probable, as the symptoms of stasis in the territory of the portal vein usually fall into the background in suppurative pylephlebitis.

Icterus.—If we disregard those cases in which intense jaundice is a symptom of a disease of the biliary passages (closure of the ductus hepaticus and choledochus by calculi, cholangitis ulcerosa, etc.), which has caused the pylephlebitis, icterus is not by any means a constant symptom of the latter affection. It is entirely absent in a fourth of the patients, and even in those who present extensive abscess-formation in the liver. Jaundice does not appear in the beginning of the disease, but only after it has lasted for some time. The color of the skin is either very pale yellow, a deep citron yellow, or, at times, even greenish. The causation of the jaundice is not the same in all cases of pylephlebitis. As a rule, it belongs to the true hepatogenic variety, dependent upon compression of the hepatic bile-ducts by the thickened branches of the portal vein in their vicinity, or upon the spread of the inflammatory process from the diseased vessels

to the accompanying bile-ducts, upon swelling of the mucous membrane of the latter, etc. As a rule, however, the closure of the bile-ducts is not complete, as the fæces rarely appear entirely colorless. Under these circumstances, the urine presents a decided brownish color, and the presence of biliary coloring matters may be demonstrated by the ordinary reagents. In other cases, however, in which the discoloration of the skin only appears in the later stages of the disease and remains of a pale yellow, we have to deal with hematogenic icterus, such as is often seen in septic diseased conditions, etc. In such an event the urine is orange-colored, contains no trace of biliary coloring matter, and the passages have the ordinary biliary appearance. The icterus also causes the ecchymoses in the integument of the lower limbs and other parts of the body which have been observed in some patients (Dance, Waller, and others).

The functions of the digestive apparatus are always markedly disturbed in suppurative pylephlebitis. On the part of the stomach we notice complete anorexia, nausea, and repeated vomiting of greenish masses (in about one-fourth of the patients) —symptoms such as are observed in acute gastric catarrh. The vomiting is, perhaps, attributable rather to the peritonitis which extends over the stomach. The formation of aphthæ noticed by some observers upon the buccal mucous membrane is not connected with pylephlebitis as such, but simply indicates that we have to deal with extremely debilitated patients who lie with open mouths and neglect cleansing the buccal cavity.

The intestinal symptoms are more important. The majority of patients suffer from diarrhœa (bile-stained), which begins soon after the pylephlebitis, and may be explained by the venous congestion of the intestinal mucous membrane, which is a necessary consequence of the impermeability of the portal vein. The stools are sometimes mixed with a little blood, but profuse hemorrhages from the intestinal canal have not been observed. In cases in which the diarrhœa only develops in the later stages of pylephlebitis it may be regarded as a sign of septicæmia. Constipation is only observed exceptionally and temporarily.

The signs of peritonitis develop quite frequently in the course of pylephlebitis. It may be confined for a long time to the primary

diseased process upon the cæcum, the umbilicus, etc. It then spreads gradually over the abdomen, but is rarely diffused at once. The abdomen is distended, there is a certain degree of meteorism, the abdominal walls are tense, the abdomen painful. The meteorism sometimes attains a very high grade, and is occasionally present from the onset of the disease. The peritonitis gives rise to the emesis of greenish masses previously mentioned, and especially to the alternation of diarrhœa and constipation, which precedes the colliquative diarrhœa of the final period.

Some observers have found dilatation of the subcutaneous veins of the abdominal walls in suppurative pylephlebitis; the majority, however, explicitly mention the absence of this condition. When the disease runs a rapid course, sufficient time does not elapse for the development of this condition, but the signs of the compensatory circulation usually develop to a greater or less extent when the course is protracted. Similar remarks will hold good with regard to ascites. The quantity of fluid found in the abdominal cavity in pylephlebitis is rarely excessive. Moreover, this is not always a purely serous transudation, *i.e.*, a symptom of stasis, but the fluid collected in the abdominal cavity often presents the characteristics of inflammatory dropsy.

During the course of suppurative pylephlebitis the urine is excreted in smaller quantity, and finally it ceases almost entirely, although there has been no noteworthy disturbance of the kidneys. If icterus is present, the urine presents the well-known brownish color; in other cases nothing especial can be noticed. The later French writers on pylephlebitis have paid considerable attention to the diminished amount of urea in the urine. They refer to the views of Charcot with regard to intermittent hepatic fever (compare page 755), and discuss the question whether there is a causal connection and what its character between the acute diminution of the quantity of urea and the febrile paroxysms of purulent pylephlebitis, which are often like those of intermittent fever. The question has not, by any means, been settled. In the first place, further observations must be made with regard to the excretion of urine in this relatively rare affection. In a patient of Le Dieu the amount of urea in twenty-four hours barely amounted to 16 grammes, while in healthy adults, under ordi-

nary circumstances and when taking abundant food, it amounts to from 30 to 40 grammes (in the fasting condition, 17), and increases, in febrile conditions, to twice this quantity, or even more. Quénu found only 10 grammes in one litre of urine, although the patient excreted very little.

Fever and other general disturbances constitute the chief symptoms in the clinical history of purulent pylephlebitis, and are the only absolutely constant features of the disease. We do not feel tempted to enter into an explanation of the origin of the fever and the peculiar chills, as we can scarcely offer more than surmises. We leave it undecided whether the chills, especially the first one, depend upon the mixture of the pyrogenic substances present in the diseased vein, with the general mass of blood, or whether this symptom indicates the entrance of pus and diseased particles of thrombus into the liver, and, on the whole, what part is taken by the liver in the development of these chills.

The first chill is an indication that the suppuration has begun in the vein, and that the disease has taken an unfavorable turn. The subsequent ones sometimes appear with an irregularity which reminds us of intermittent fever, except that they occur at any part of the day or night. Quinine is always useless in combating them. Usually, however, they soon become irregular, are repeated several times a day, and on other days are entirely absent. They are followed by great heat and profuse exhausting perspiration; the hot stage is rarely absent after the chill. When the disease is protracted, the fever, after a few paroxysms, assumes the remittent type with nocturnal exacerbations, and, at the same time, a hectic character. The increase of temperature corresponding to the chill rises beyond 104.° F., and often reaches 105.8° F., even 106.8° F. The frequency of the pulse varies between 90 and 130 beats.

Not less characteristic than the fever is the rapid emaciation of the body and the rapid loss of power.

In the majority of cases severe typhoid symptoms on the part of the nervous system (disturbances of the sensorium, delirium, somnolence, etc.) develop, as in septic conditions generally, in the later stages of suppurative pylephlebitis. Only in excep-

tional instances does the patient retain consciousness until death.

Pains in the chest, disturbances of respiration, bloody sputum, and other signs of a disease of the lungs and pleura, also pains and swelling of individual joints—symptoms, therefore, which are produced by pyæmic metastases, only occur in exceptional cases, as we have previously mentioned. As a rule, however, the anatomical lesions peculiar to pyæmia do not extend, in suppurative pylephlebitis, beyond the territory of the portal vein.

Diagnosis.

The difficulties of diagnosis are regarded in various lights. While some consider it a rare stroke of good fortune to recognize the disease, others maintain that nothing is simpler and easier than the diagnosis of suppurative pylephlebitis. If we examine individual cases unbiassedly, we must acknowledge that both opinions are correct, in so far as we do not claim general acceptance for them, but restrict them to concrete examples.

There are no definite pathognomonic signs by which we can recognize the disease under all circumstances. The diagnosis must be based upon the ensemble of the symptoms, upon the sequence of their appearance, and in general upon the development of the phenomena. If this is done, and all the essential symptoms are really present, the diagnosis of pylephlebitis will not be attended with special difficulty, particularly when the pre-existing and underlying affections have been properly considered and employed in making the diagnosis.[1]

The following are the most important factors upon which the diagnosis should be based :

1. The presence of an affection which we know, from experience, may act as the starting-point and exciting cause of pylephlebitis, especially perityphlitis, a purulent focus or an ulceration of the stomach, intestine, rectum, spleen, the biliary passa-

[1] Compare the instructive views of *Traube*, communicated by *Fraentzel*, Berl. klin. Wschr., 1869, S. 4 u. 13.

ges, the umbilicus of the new-born, furthermore, a chronic peritonitis, etc.

2. Pain in the epigastrium, above the umbilicus, and in the right hypochondrium, or any other situation in which the pylephlebitis may start.

3. Violent chills, which are repeated at irregular intervals and are followed by great heat and profuse sweats, while the temperature in the intermission remains abnormally high (and pyæmia, in the ordinary surgical sense, is excluded).

4. The recent, uniform, and painful enlargement of the liver. Enlargement of the organ is not constant, but tenderness is always present.

5. Considerable enlargement of the spleen, especially when we can follow its development.

6. The icteric color of the skin and urine in addition to the biliary diarrhœa.

7. Rapid emaciation of the body and profound loss of power.

8. The occasional development of diffuse peritonitis and typhoid symptoms in the later stages of the disease.

When these symptoms are combined, the diagnosis of suppurative pylephlebitis, as we have stated above, may be regarded as certain. But the majority of the above-mentioned symptoms may be absent singly or in groups, and then, under certain circumstances, the diagnosis may become impossible, or we must rest satisfied with a more or less probable suspicion of pylephlebitis.

Thus, for instance, I recently had under observation a child, about three weeks old, who died of pylephlebitis of the branches of the portal vein, in the right lobe of the liver, and of the trunk of the vessel, in whom no inflammation of the umbilicus, no enlargement of the liver, no icterus, no well-developed chills were observed, nor were there any signs of peritonitis or any marked emaciation. Apart from the indications of something wrong, nothing could be noticed objectively, except fever, with marked remissions, and moderate enlargement of the liver. These factors were, naturally, insufficient to form a diagnosis of pylephlebitis.

The following are the diseases for which purulent inflammation of the portal vein may be mistaken, especially in the begin-

ning of the disease, or when the patient is not under observation during its entire course:

a. *Catarrhal icterus* (compare Fraentzel, l. c.). This presents, in addition to the yellow color of the skin, etc., the enlargement and tenderness of the liver, sometimes the enlargement of the spleen, and may also be accompanied by fever. But, in the latter, the severe chills, much less the extreme and rapid emaciation and profound loss of power, will not appear; these indicate a much more serious disease than catarrhal jaundice.

b. *Chronic blennorrhœa of the biliary passages* may be especially mistaken for those cases of pylephlebitis which are due to gall-stones and ulcerative cholangitis. Chills, icterus, and enlargement of the liver occur in blennorrhœa of the biliary passages as in pylephlebitis. But the enlargement of the spleen is absent, or does not attain the same dimensions as in the latter disease, and its course is more latent, the emaciation and prostration do not, by any means, reach the same grade as in pylephlebitis.

c. *Closure of the bile-ducts by calculi* resembles pylephlebitis with regard to jaundice, the enlarged and painful liver, the irregular chills. In the former we miss the diarrhœa, the enlargement of the spleen, the septic infection, the rapid emaciation; the stools are colorless in closure of the bile-ducts, and bile-stained in pylephlebitis.

d. *Idiopathic abscess of the liver* presents, in common with pylephlebitis, enlargement of the organ, tenderness, chills and fever. But the causes of both diseases are entirely different; in hepatic abscess the enlargement of the spleen is absent, as are also the diarrhœa, rapid emaciation, and extreme prostration; the pyæmic condition, which is observed, as a rule, in pylephlebitis, is uniformly absent in hepatic abscess.

e. *Intermittent fever* may, for a time, be mistaken for pylephlebitis, on account of the chills followed by the hot and sweating stage and the enlargement of the liver. With reference to the remaining symptoms, these diseases have nothing in common with one another, and even with regard to the chills the uselessness of quinine prevents a long-continued confusion with intermittent fever.

The majority of authors also discuss the differential diagnosis of adhesive and suppurative pylephlebitis, as if these diseases were very similar to one another, although, in fact, they have hardly one symptom in common. We regard this view as the residue of the former but now discarded notion, which considered both diseases from the common standpoint of pylephlebitis.

Course, Duration, Terminations.

The course of purulent pylephlebitis is either acute or subacute. In the majority of cases there is an interval of about fourteen days between the first chill and the fatal termination. Its course is sometimes shorter, and only lasts for a few days; but cases are by no means rare in which the disease has a duration of four to six weeks. Some authors even regard this as the rule (Traube). Only in exceptional instances does pylephlebitis extend over a longer period. Leudet mentions a case in which the disease only reached its termination in five months. It is evident that this is only possible when the affection does not assume a septic character.

We only know one termination of suppurative pylephlebitis, viz., in death. The septic infection of the blood and the extreme exhaustion in consequence of fever, etc., must be regarded as the chief causes of the fatal termination.

Prognosis.

In developed cases of purulent inflammation of the portal vein the prognosis is absolutely fatal. At the best, the possibility of recovery can only be thought of in a case in which phlebitis involves some branches of the portal vein of restricted extent, and in which the trunk and hepatic branches are not implicated. But this will only hold good when the circumscribed phlebitis does not present a septic character.

Treatment.

We are entirely impotent against purulent pylephlebitis, as we can obtain no influence over the diseased process, nor can we prevent septic infection of the entire organism by the local process. It would therefore be useless to combat inflammation of the portal vein by local measures. Venesection would not alone be useless, but positively injurious by hastening the exhaustion of the patient. We are therefore restricted to symptomatic measures. The end in view consists in relieving the complaints of the patient as much as possible, and making his subjective condition comfortable. We should endeavor to combat the pains and diarrhœa by opiates, the threatened loss of nutrition by strong wine, etc. Very little can be said against the use of quinine and salicylic acid as antipyretics. Although quinine has proven ineffectual in the chills of suppurative pylephlebitis, it may nevertheless be tried, as a mistake may have been made in diagnosis, and we may have to deal with a disease in which quinine does good service.

Cancer of the Portal Vein.

(Pylethrombosis carcinomatosa.)

Carswell, Illustrat. of the Elementary Forms of Disease. London, 1838. Carcinoma. Plate III., Figs. 2 and 4; Plate IV., Fig. 4.—*Puchelt,* Das Venensystem in seinen Krankhaften Verhältnissen. 2 Aufl. Leipzig, 1844.—*Virchow,* Arch. f. path. Anat. II., S. 597.—*Meyer,* Ueber Krebsige Phlebitis, Ztschr. f. rat. Med. N. F. III. 1853. S. 136.—*Bamberger,* Krankh. d. chylopöet. Systems, Virch. Handb. d. Path. u. Ther. IV., 1. 1855. S. 638.—*Frerichs,* Klinik d. Leberkrankh. II. S. 278.—*Findeisen,* Ueber carcinomatöse Thrombose d. Pfortader Dissert. Jena, 1863.—*Spaeth,* Carcinom im Innern der Venen des Pfortadergebiets, Virch. Arch. XXXV. S. 432 (1866). *Paulicki,* Thrombose d. Pfortader durch Krebs, etc. Berl. klin. Wchschr. 1869. S. 393.

The older observers made no clear distinction between simple thrombosis of the portal vein and filling of its lumen with cancerous masses, because they assumed, either outspokenly or

tacitly, that it was possible for a thrombus within the vein to undergo "organization into cancerous masses," and because there was no clinical necessity for such a differentiation. Whoever desires to become acquainted with the old cases of portal cancer must also look through the literature of (adhesive) pylephlebitis.

Cancer of the portal vein is not an independent disease, but always supervenes upon cancer of the stomach, intestines, liver, or, in general, upon a carcinoma in the territory of the portal vein. The primary growth, which starts from one of the above-mentioned organs, spreads to the wall of one of the veins in the territory of the vena porta, grows into its lumen, fills it completely, and becomes organically united with its wall, as the vasa vasorum of the latter unite with the blood-vessels of the intravenous cancer nodules; it grows rapidly in two directions along the lumen of the vein, either with or against the current of blood. Thus, the cancer, for example, may grow from the gastric veins into the trunk of the portal vein, and from the latter backward into the roots of the vena mesenterica, lienalis, etc. From the trunk it grows centrally into individual hepatic branches, and finally spreads from these into the surrounding hepatic parenchyma, so that it is at times impossible to clearly recognize the walls of the branches of the portal veins in the cancerous masses.

Primary cancer of the liver rarely penetrates into the adjacent portal veins, and then spreads backward into the trunk and roots of the vena porta.

A few observations have, however, been made by reliable authorities, according to which it appears that the cancer elements may develop from the constituents of the blood within the vessels, independently of a pre-existing carcinoma. An instance of this kind is reported by Virchow,[1] and Bamberger also mentions a case (l. c., S. 638), in which, although no cancerous deposit was previously present in the organism, the entire portal vein, even into its finest ramifications, was filled with a

[1] Arch. d. path. Anat., II., 1849, S. 597; Gesammelte Abhandlgn., Frankfort, 1856, S. 350, u. 551 ff.

pulpy coagulum which was entirely formed of large nucleated cells of various forms.

However strange these statements may appear at first sight, and however opposed to the modern views with regard to cancer they appear to be, they may be readily explained from this very standpoint. These observations could not, indeed, have referred to cancers in the modern sense—*i.e.*, to those of epithelial origin. If we assume, however, that the masses of cells collected in the veins possessed a medullary sarcomatous character, as the caudate bodies in Virchow's case appear to indicate, there is nothing inexplicable in these cases even to our modern views. All observers are of the opinion that medullary sarcoma, as well as cancer of epithelial origin, may appear under the form of "venous cancer." However, Virchow's and Bamberger's cases must be regarded as rare exceptions, which do not change the fact that cancer of the portal vein is, as a rule, secondary, and is in continuous communication with a primary carcinomatous neoplasm of the stomach, or some organ in the territory of the portal vein.

The distribution of cancer of the portal vein presents the greatest variations. As a rule, in addition to one of the radicles, the trunk, and the hepatic branches or some of the latter, are filled with cancerous masses. Sometimes, however, we find all the radicles of the portal vein, back to their very beginning, filled with cancer tissue.

The veins affected by the cancer are markedly thickened, and the trunk of the portal vein is fully as thick as a man's thumb. The diseased vessels appear as firm cords, their connective-tissue sheath is very vascular, the wall of the vein more or less thickened—otherwise scarcely changed to the naked eye, at least externally. The vein contains a soft, creamy white to reddish mass, or is filled with a white mass of tissue which possesses the consistence of ordinary medullary cancer, or of carcinoma simplex. The carcinomatous creamy contents may occasionally be regarded in the smaller vessels as simple cancer-juice—*i.e.*, it merely consists of cancer-cells without the vascular connective-tissue stroma, and in this event the tunica intima of the affected vein appears smooth and intact. In general, however, cancer of

the veins, like cancer in any other portion of the body, is provided with a connective-tissue stroma, and with fine vessels in the axis of the bands of stroma. The vessels of the intravenous cancer stroma are then continuous with the strongly-developed vasa vasorum of the walls of the vein, so that the latter forms an organic whole with the cancer inside.

As soon as the primary cancer has ruptured into one of the veins belonging to the portal system, the spread of the new formation within the vessels occurs with extreme rapidity. After a certain lapse of time, therefore, the signs of portal occlusion usually become very prominent, at first within the territory of the venous radicle primarily affected, but soon after, when the trunk of the vena porta is affected, throughout the entire domain of the portal system.

The resulting symptoms coincide exactly with those of simple pylethrombosis, as it is immaterial with regard to the mechanical consequences whether the lumen of the vessels is occluded by a blood-clot or by a mass of cancer. With regard to these symptoms, therefore, we refer to the description which we have given of the phenomena of pylethrombosis.

The same general rules hold good with regard to the diagnosis of portal cancer as of pylethrombosis, with the reservation, however, that we may only assume cancerous occlusion of the vessel when the existence of a cancer in the territory of the radicles of the portal vein has either been proven, or, at least, rendered highly probable.

As we have previously stated, cancer of the portal vein develops with comparative rapidity ; its duration is not often prolonged beyond a period of from fourteen days to four weeks. As a matter of course, the prognosis is fatal. There can hardly be any question of treatment. The indications are limited to alleviation of the most distressing symptoms and to euthanasia.

The remaining diseased processes of the portal vein are of minor clinical importance, and only excite our interest from the standpoint of pathological anatomy. The following are the most noteworthy :

1. *Dilatation of the Portal Vein (Pylephlebectasis).*

This is observed quite rarely, either in the trunk or the radicles of the vessel; it may be uniform and diffuse (in which event the vein is enlarged to twice its normal diameter, or even more, and its radicles are especially sinuous), or it is circumscribed, sacculated, or varicose.[1] The dilatation is usually the result of impermeability of the hepatic branches or the trunk of the portal vein, and must therefore be regarded as an expression of stasis of blood. More rarely it may be due to local nutritive disturbances in the walls of the vein, to chronic inflammation of the latter, etc. It is also seen occasionally in young persons. Neelsen,[2] who found in an imbecile, æt. fifty-seven years, the subserous veins of the colon strewn with dark red, mulberry-shaped varices, from the size of a grain of wheat to that of a large pea, is of the opinion that a mechanical cause of such varicosities cannot always be discovered; that we should rather think of nervous influences by which an abolition of the walls of the vein is produced. The latter method of development alone is said to hold good for varices of the portal vein.

2. *Chronic Pylephlebitis (Calcification and Ossification of the Portal Vein).*[3]

This is especially observed in a circumscribed manner in the portal vein, leads to fibrous thickening of the venous walls, which sometimes starts from the tunica intima of the vessel, sometimes from the connective-tissue sheath, and, in its further course, usually leads to calcification and ossification of the walls. Chronic pylephlebitis is almost always combined with thrombosis in the territory of the affected portion of the vessel. The causal relation between both conditions may, as a rule, be interpreted as follows: the thrombosis is the primary change and

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[1] Compare *Virchow's* case, referred to on p. 790.

[2] Beitrag zur Kenntniss der Varicen im Gebiete der Pfortader. Berl. klin. Wochenschr., 1879, Nos. 30, 31 (compare *Virchow* and *Hirsch*, Jahresber. f. 1879, I., S. 232).

[3] Compare *Frerichs*, Kl. d. Leberkrnkhtn., II., S. 380. *Phoebus*, De concrementis venarum osseis et calculosis. Inaugural Thesis, Berlin, 1832.

the cause of the chronic inflammatory disturbance of nutrition. On the other hand, we cannot deny the possibility that the affection of the wall of the vein is the exciting cause of the coagulation of blood. A remarkable example of this chronic pylephlebitis is presented in the case described by Virchow,[1] which has been previously referred to (compare p. 790). The inner coat of the trunk of the portal vein attained the thickness of one centimetre; it was of a brawny, semi-cartilaginous consistence, and had considerably narrowed the lumen of the vessel. The cause of this venous affection was considered by Virchow to be the irritation produced upon the adjacent walls of the portal vein by the pressure of gall-stones that had probably been situated in the ductus choledochus.

3. *Rupture of the Portal Vein.*

This is a very rare phenomenon. We do not now refer to traumatic ruptures; but so-called spontaneous ruptures of the portal vein (as a rule, the trunk, more rarely the radicles) also occur, the causes of which must be sought for in profound nutritive disturbances of the walls. Frerichs[2] observed a case of this kind in a man æt. forty-one years:

The trunk of the portal and the splenic veins, together with smaller branches, were in an advanced stage of fatty degeneration, soft, and easily torn. A large extravasation of blood lay between the layers of peritoneum which enclosed the portal and splenic veins. No rupture could be found in the vessels just mentioned, but the source of the hemorrhage appeared to be in the smaller branches, especially the short gastric veins and the branches of the right coronary vein, as these were lost in the mass of coagulated blood. The patient, who was addicted to drink, experienced a sensation, during a cardialgic attack, as if something had torn in the upper portion of the abdomen, and as if a fluid had escaped. Soon afterward he became weak, fainted, the abdomen became tense and distended; the pyloric and ileo-cæcal regions were painful. Death occurred about sixty hours after the development of the symptoms mentioned.

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[1] Verhandln. d. phys.-med. Ges. z. Würzburg, VIII., S. 22. *Frerichs*, Kl. d. Leberkrankhtn., II., S. 369.

[2] L. c., S. 382, where other cases of spontaneous rupture of the portal vein (in former times) are mentioned.

4. *Foreign Bodies, Gall-Stones, and Distomata in the Portal Vein.*

Remarks regarding the presence of gall-stones in the portal vein are found upon p. 731. Deway's observation, which is mentioned there, demonstrates with reasonable certainty the occurrence of this surprising phenomenon.

The observation of Duval[1] in 1830, with regard to parasites of the portal vein, is a unique one. During an anatomical demonstration upon the body of a man, æt. forty-nine years, concerning whose antecedents nothing could be discovered, this writer accidentally found five or six well-preserved distomata (d. hepaticum) in the fluid blood of the portal vein, one of them being in the trunk, the others in the hepatic branches. The radicles of the portal vein contained no distomata. The liver and portal vein presented an entirely normal appearance.

The distomata hæmatobium possesses the greatest pathological significance in the human species. This variety, especially indigenous in Egypt, is found in the trunk and branches of the portal vein, the hepatic and mesenteric veins, the rectal and vesical plexuses, and is nourished by the blood. It is well known that these worms become especially dangerous, because they deposit their ova in the mucous membrane of the urinary passages, give rise to inflammation of these parts, to hæmaturia, formation of calculi, etc. It is probable, however, that the portal vein does not escape unscathed, though there are no positive statements concerning anatomo-pathological changes of the portal vein due to distoma hæmatobium. Some remarks of Griesinger, and the fact that this worm deposits its ova in masses in the liver, between the intestinal walls, etc., make it appear probable that the bad consequences are not restricted to the urinary passages, but that anatomical changes are also produced in the territory of the portal vein.[2]

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[1] Gaz. méd. de Paris, 1842, p. 769. Compare *Davaine*, Traité d. Entozoaires, 2 éd., 1877, p. 322.

[2] *Leuckart*, Die menschl. Parasiten. I., S. 619.

The Diseases of the Hepatic Veins

have not attained an independent position in clinical treatises, although they are not extremely rare or unimportant. The most frequent change consists of *diffuse dilatation*, which develops from stasis of blood in the veins of the body, and in various cardiac and hepatic diseases.

Purulent phlebitis, the most frequent form of inflammation of the hepatic veins, may always be attributed to the presence of abscesses in the liver. Idiopathic hepatic abscess, as well as pyæmic (metastatic) abscesses, and those occurring in consequence of suppurative pylephlebitis, may spread to the veins mentioned so much more readily, as they are destitute of a separate sheath.[1]

Coagulation of blood first occurs in the affected veins, the thrombus undergoes puriform softening, and the thin wall of the inflamed hepatic vein rapidly becomes subject to necrosis and ulcerative degeneration. Removal of particles of the thrombus may readily occur, and thus lead to infection of the entire mass of blood, and to formation of metastatic foci in the lungs, spleen, and other organs. The implication of the hepatic veins in the suppurative process cannot readily be detected at the bedside.

Adhesive phlebitis hepatica, which is, on the whole, a rare disease, only involves individual hepatic veins, while the others remain unaffected. The spread of inflammations of the serous covering of the liver, and of that portion at which it bends over upon the diaphragm to the wall of the veins, is stated to be the most frequent cause.[2]

I recently observed the disease in question in an autopsy upon an individual sixteen years old, in whom the superior longitudinal and both transverse sinuses of the dura mater were occluded by a completely organized thrombus. The patient, who suffered considerably from headache, died of acute sero-fibrinous pleurisy of the right side. The liver was quite large, several large veins of the right lobe were completely filled and entirely obliterated by œdematous connective-tissue masses, almost destitute of pigment, and organically united to the walls of the veins. The spleen very much enlarged, twenty centimetres long; no ascites.

[1] Compare *Bristowe*, Path. Trans., Vol. IX., 1858, p. 283.

[2] *Frerichs*, Kl. d. Leberkrankhtn., II., S. 408.

In this case the capsule of the liver was normal, and the hepatic tissue showed very slight changes in the territory of the occluded veins, which were recognized as the results of the vascular occlusion. In the absence of any mechanical cause we must adopt the view that perhaps a change in the constitution of the blood, a greater tendency to coagulation, or something of that nature, may have been the cause of adhesive phlebitis hepatica, and presumably also of the thrombosis of the sinuses of the dura mater.

As the obliteration of the hepatic veins causes destruction of the capillary territory of the corresponding hepatic lobule (at first in the centre of the acini), and atrophy of the hepatic cells, the flow of blood from the hepatic branches of the portal vein must be interfered with, and, in addition, symptoms of stasis in the territory of the portal vein may develop, as in occlusion of the vena porta. But even if these sequelæ did result, it would not be possible to recognize adhesive phlebitis hepatica at the bedside, or to distinguish it from portal occlusion.

Cancer of the hepatic veins is observed quite frequently by careful anatomists; it is always a sequence of cancerous infiltration of the liver. All forms of hepatic cancer, primary and secondary, infiltrated and nodular, may occasionally spread to the hepatic veins and fill their lumen over a considerable area. I have not, however, observed this condition in colloid cancer of the liver. The clinical history of hepatic cancer is not changed by the fact that the new-growth spreads to the hepatic veins and occludes their lumen. Cancerous thrombosis presents, therefore, only an anatomical interest.

For the sake of completeness we will also refer to diseases of the hepatic artery. The atheromatous process, which occurs in this vessel as well as in others, presents no peculiarities. Some interest attaches, however, to

Aneurism of the Hepatic Artery.

Among the older cases, which had already been discussed by Frerichs, only three are of clinical importance,[1] viz., those of

[1] One of the cases in *Stokes* (Diseases of the Heart), that of *Ledieu* (Journ. de Bordeaux, Mars, 1856), of *Sestié* (Bull. de la soc. anat., 1833), and of *Wilson* (Med.-Chir. Trans., 1841, XXIV.), possess, at the most, an anatomical interest, but are otherwise

Stokes, Wallmann, and Lebert. To these may be added two other well observed and clinically interesting cases, which were described by Quincke and Borchers, while two other cases constitute merely accidental autopsical discoveries. The material which can be utilized is therefore restricted to the following:

1. Stokes (Diseases of the Heart, p. 638). Patient, æt. thirty-five years. An aneurismal sac, as large as an orange, beneath the liver, which had pressed upon the bile-duct, finally opens into the latter. Sudden death. The intestines filled with fresh blood. During life the aneurismal tumor had been felt in the region of the left lobe of the liver, together with the enlarged gall-bladder. Long-continued hæmatemesis. Icterus.

2. Wallmann (Virch. Arch., XIV., S. 389). Woman, æt. thirty-six years. The aneurism of the hepatic artery forms an ovoid tumor as large as a child's head, situated between the liver and stomach. It is ruptured at the lower end; extravasation of blood into the abdominal cavity. The biliary passages are enclosed in the anterior wall of the sac. During life severe attacks of pain had been felt for a long time in the upper part of the abdomen; icterus ten days before death. Sudden collapse and death, with abdominal distention.

3. Lebert (Traité d'anat. path. T. II., p. 322). Woman, æt. thirty years. Pain and pressure in the gastric region, copious and repeated hæmatemesis, and bloody stools, which could not be relieved. Extreme anæmia; death from exhaustion. An aneurism of the hepatic artery as large as a pigeon's egg was adherent to the gall-bladder and had opened into it.

4. Quincke (Berl. klin. Wochenschr., 1871). Man, æt. twenty-five years. Hemorrhages from the intestines and icterus appear and disappear several times during a number of months. Severe, pressing pains also developed in the epigastrium. Repeated hæmatemesis. Death occurred from exhaustion, after enormous losses of blood in the stools. An aneurism of the right branch of the hepatic artery, as large as a chestnut, is enclosed in the parenchyma of the liver. It is situated in the lumen of the right branch of the hepatic duct, immediately adjacent, and which is entirely occluded thereby. No perforation could be found.

5. Borchers (Aneurysma d. Art. hepat. Diss. Kiel, 1878). Man, æt. seventeen years. Sudden, acute pains in epigastrium; repeated hæmatemesis. Icterus. Death in consequence of amputation of the femur. Two aneurismal sacs (2.2 and 2.5 ctm. in diameter) within the liver upon the trunk of the hepatic artery. One aneurismal sac has ruptured into the adjacent hepatic duct.

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of minor importance. The more recent cases, which cannot be utilized for our purposes, are those of *Staudthartner* (Ber. d. Wien. allg. Krankenhauses, 1875), and *Ross* and *Osler* (Canada Med. and Surg. Journ., July, 1877).

From this material, it appears, as Frerichs (l. c., II., S. 363) had previously shown, that the chief symptoms of aneurism of the hepatic artery are three-fold. The most important is the tumor, which was considerable in two cases and even dislocated the liver, but was absent in smaller ones and in those situated within the liver. Another important symptom is the pain, which is neuralgic in character and occurs paroxysmally, or at least exacerbates like a paroxysm. This must be attributed to the irritation of the hepatic plexus by the pressure of the aneurismal sac. The third symptom, viz., jaundice, can in like manner be explained by the compression of the biliary passages by the arterial tumor. The enormous losses of blood, which are noticed in the majority of cases, may, indeed, aid the diagnosis of an aneurism which has perforated the biliary passages, but they may also lead to the suspicion of a chronic gastric ulcer; indeed, aneurism of the hepatic artery may readily be mistaken for the latter affection or for biliary colic. In the majority of cases death occurs from hemorrhage. In the case reported by Ross and Osler, the patient died of multiple hepatic abscesses, which are said to have been produced by the removal of particles of fibrin from the aneurismal sac into the finer arterial branches of the liver.

INTERSTITIAL PNEUMONIA.

CIRRHOSIS OF THE LUNGS AND BRONCHIECTASIS.

JUERGENSEN.

INTERSTITIAL PNEUMONIA, CIRRHOSIS, AND BRONCHIECTASIS.

References to the literature of the subject will be found in Vol. V. under the headings of the diseases of the lungs already treated of, and also in the body of the present article. For Bronchiectasis see the article by Biermer in Virchow's Handbuch der speciellen Pathologie und Therapie. Bd. V., S. 134 and 135.

The results of those inflammatory processes which take place in the connective-tissue framework of the lung are designated by the name of interstitial pneumonia.

This disease, we may safely say, never occurs independently. On the contrary, it frequently accompanies many of the most common bronchial pulmonary affections. Often, however, the interstitial pneumonia is associated with the original disease in such a way that the character of the latter is scarcely influenced by it, and its presence may be surmised more on general principles than by any actual demonstrable lesions.

On the other hand, certain sequelæ and results of interstitial pneumonia,—as, for example, contraction of the lung and dilatation of the bronchi,—may present symptoms so strikingly characteristic that these completely overshadow those of the original malady.

In reality, *interstitial pneumonia is not a clinical but rather an anatomical entity*, the forms under which it appears being such as cannot well be confined by any fixed, immutable set of rules, but are, on the contrary, subject to the greatest degree of variability. The original malady and its sequela of interstitial pneumonia are, furthermore, so intimately interwoven, that any one-sided attempt to separate the two, and consider each with-

out its relation to the other, would only lead us into error and confusion. A purely schematic representation, therefore, even though it might succeed in giving to a description of this pulmonary disease an apparent though really deceptive clearness, would only be fraught with evil, and be worse than useless to the physician.

Interstitial pneumonia is a sort of borderland on which opposing factions of observers wage their war of theories. In this respect it is like phthisis. Indeed, it is hardly probable that a satisfactory explanation of the cause or causes of interstitial pneumonia will be forthcoming any sooner than the solution of the purely anatomical problem of the occurrence and the significance of tubercle, and its anatomico-clinical relations to phthisis.

One is so apt to fall into the error of contrasting and comparing with each other things which in reality have no rational relationship, that we shall in future try, wrongly perhaps, to evade this danger by avoiding any too sharply defined descriptions.

I think it but right to premise these remarks, in order to ask of my associates a more correct consideration of my views than they might otherwise accord to me.

History.[1]

In taking up the literature of the subject, we find that the earlier observers confined their attention more to all the possible consequences of interstitial pneumonia than to the disease itself. It is in Laennec that we find the first description of dilatation of the bronchi (bronchiectasis), which intelligently separates this condition from those related to it. Laennec tells how his attention was first drawn to it by Cayol, at that time a student, but afterward professor of medicine, who was "astonished at finding a diseased state of the lung, which, up to that time, had remained undescribed."[2] This, it appears from Laennec, was in 1808.[3]

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[1] Without having neglected the earlier sources of information, I have substantially followed *Biermer*, whose observations throughout have been found to be correct.

[2] l. c., Vol. I., p. 168.

[3] *Id.*, Case I.: Bronchiectasis following Whooping-cough.

When we take into consideration his very meagre material—but four cases—it is remarkable what an admirable account, anatomically considered, Laennec gave of this new disease. And while clinically it is correct in all the most important features, the only defective point of the description lies in the misinterpretation of the newly discovered facts.

In it the various forms of bronchial dilatations, the indurated condition of the lung-tissue surrounding them, and the changes which a lung in this state presents, were all so accurately, and even minutely, described, that many details were alluded to whose significance was only recognized and understood at a considerably later period.

Laennec attributes the formation of bronchiectatic cavities to a mechanical cause, namely, to the pressure exerted by the mucous secretion from the bronchi, such as occurs in chronic catarrh.

"It is impossible," he says, "for a considerable amount of the products of secretion to accumulate at one spot in a bronchus, and remain there any length of time, without causing a dilatation; and if, after the accumulated mass has been expelled, a new collection forms at the same place from a fresh secretion of material, it is evident that the dilatation will have a tendency to become permanent; and, according to circumstances not yet understood in the present state of medical science, either a permanent hypertrophy or an atrophy of the affected mucous membrane will result." [1]

It appears quite evident from the above that Laennec in no wise claimed to have given an exhaustive explanation of this disease.

Andral, who generally agrees with his celebrated countryman, has nevertheless called attention to the fact that Laennec sometimes represented things rather as he presupposed them to be than they actually were, as proved by observation.

Like Laennec, Andral too had but few cases on which to make his observations, the number in his case being limited to five.

He supplements Laennec's explanations by showing that, in addition to the other causes, disturbances of nutrition occurring in the walls of the bronchi play a not unimportant part in the formation of bronchiectatic cavities.[2] Furthermore, from one of

[1] l. c., p. 165.

[2] Clinique médic., Vol. III., p. 199.

his observations (No. IX.), he is enabled to call attention to the fact that in the slighter grades the clinical signs of bronchiectasis may be wanting.

Reynaud's observations next appeared. In his work on bronchial stenoses[1] we find the conviction expressed that respiration is concerned in the formation of bronchiectases. This opinion is arrived at from observing the fact that dilatations are found both above and below contracted portions of the bronchial tubes. He says:[2]

"On the other hand, inspiratory pressure, or that power which permits a given volume of air to penetrate the lung as a whole, is not decreased by this circumstance (contractions of single bronchial tubes). The result is, that those portions of the bronchi lying in the immediate neighborhood of the contractions are made to dilate."

Even while we must admit that Reynaud has given undue prominence to the agency of inspiration, still the credit of having been the first to point out the mechanical forces at work during this act must always be accorded to him.

The observations of the French were followed by those of the English.

The explanation of the causes of bronchiectasis, as given by Stokes, is of such wide range, that it is found to embrace nearly all the possible circumstances that can be taken into account.

It was Stokes who first advanced the idea, so fertile of suggestions, that under certain circumstances bronchi and arteries are legitimately comparable. Guided partly by this analogy, no doubt, he gives the following as among the prominent causes of bronchiectasis: first, a diminished elasticity of the longitudinal fibres of the bronchi, (making the former correspond,—in this agreeing with Reiseissen,—with the adventitia of the arteries); secondly, a paresis of the circular muscular fibres; and finally, a diminished activity of the ciliated epithelia.

Stokes, however, even when discussing the new ideas which he advanced, is far too enlightened to undervalue the importance of those of his predecessors.

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[1] Mémoires de l'académie royale de médecine. Tom. IV., Paris, 1835, p. 117 sqq.
[2] l. c., pp. 152, 153.

Williams, another observer, is of opinion that a disturbance in the nutrition of the tissues, such as happens during a long-continued bronchial catarrh, may be looked upon as a favoring condition for the production of a dilatation. But this certainly cannot in any way be regarded as a satisfactory elucidation of the problem.

Williams proposes the following explanation. The elasticity of the bronchi and their "vital" power of contracting are actively at work at each expiration. Both these properties, however, would be diminished by any prolonged inflammation of the bronchial mucous membrane, and in such portions of the lungs, therefore, where this inflammatory process was at work, expiration would be unable to exert its full power, bronchial secretion would accumulate, and the air, whether by inspiratory or expiratory pressure, would induce dilatation in bronchi, already partially inelastic and animated by a weakened muscular power.

He dwells with particular emphasis on the increase in pressure which necessarily occurs in every part of the lung, during the act of coughing.

Williams, therefore, directly opposes Reynaud in regarding the act of *expiration* as one of the principal factors in the production of dilatations.

A few moments' consideration of the above discussions, soon shows us that the main point about which everything seemed to turn was the fact of the presence of dilatations in the bronchi, while the changes in the surrounding tissues were looked upon as mere sequelæ, and of very subordinate interest.

In Corrigan we find an observer who chose a diametrically opposite course for pursuing his investigations. He saw in the state of things found in the lungs about bronchial dilatations, a condition comparable to hepatic cirrhosis, and he consequently conceived the idea that the disease originally emanated from what he terms the "fibro-cellular" tissue lying between the bronchi, or, what would be, according to our nomenclature, the interstitial pulmonary connective tissue. The latter, after first undergoing inflammatory processes, gradually contracts.

"As the alveoli, the capillary bronchi and blood-vessels become obliterated, the larger bronchi are proportionally enlarged.

This enlargement takes place, not merely from an effort of the latter to occupy a space gradually increasing in size from shrinkage of the other tissues, or from an expansive force exerted upon them at every inspiration, but also because any set of tubes connected by a cellular tissue, must enlarge when this tissue contracts." [1]

Corrigan also calls particular attention to the changes which occur in the bony framework of the thorax, and to the occupancy by neighboring organs of the space left void by the contraction of the lung,—facts which his predecessors hardly alluded to.

To Corrigan, therefore, we must undoubtedly credit a very marked progress in our knowledge of the subject, and must concede the greatness of his merit as an observer, despite his sometimes one-sided conceptions.

The work just considered, establishes a sort of division in the literature of the subject, by being the first one in which the most important conditions concerned in the formation of bronchial dilatations had not only been touched upon, but even made the subject of discussion. It was reserved for Corrigan's successors to select from these conditions those belonging to particular forms of the disease or to individual cases.

This was done by those who next occupied the field, namely, the Germans Hasse [2] and Rokitansky.[3] Both of these authors dwell upon the sequelæ of interstitial pneumonia, subjects which heretofore had occupied but little attention.

Accumulation of the blood in the right side of the heart, the dilatation of the latter with or without hypertrophy, hemorrhages from the lungs, and, after a prolonged existence of the disease, finally even emaciation and dropsy, were occurrences which were not only alluded to, but even properly appreciated.

Rokitansky defined in more precise terms the idea of an "interstitial pneumonia," (which idea, though originating with his

[1] The original not being accessible, I quote from Schmidt's Jahrbücher. Bd. XX., S. 297.

[2] Anatomische Beschreibung der Krankheiten der Circulations- und Respirations-Organe. Leipzig, Engelmann, 1841. S. 400 ff.

[3] Handbuch der speciellen patholog. Anatomie. Bd. II., S. 11 ff.

predecessors,—especially Andral and Hope,—had never been clearly developed by them), traced the origin of the disease to an inflammation of the pulmonary connective tissue, and, looking at it from an anatomical point of view, treated of it as an independent lesion.[1]

The literature of the next period occupies itself with the discussion of the origin and significance of bronchiectatic cavities. And among those authors whose contributions to science are most worthy of note may be mentioned Barthez and Rilliet, Mendelssohn, Rapp, Virchow, Reinhardt, Ruehle, Gairdner, Black, Barth, van Geuns, and Bamberger. Being able to consult but few of these works in the original, I was obliged to refer to Biermer's articles,[2] in which may be found a summary of all the most important points contained in the former.

Biermer's first work appeared in 1860, and is based on very careful observations. In those volumes of Virchow's collected works, which were issued during the year 1864, a most masterly treatment of the whole subject of bronchiectasis from the pen of the former author will be found.

Our knowledge of interstitial pneumonia in still another direction has been very materially extended since 1862. About this time the attention of physicians became awakened to the kinds of diseases which the introduction of dust into the air-passages of the lungs might produce. Traube pointed out their occurrence, and Zenker positively demonstrated that the changes occurring in the lung-tissue actually did stand in the very closest relationship to the introduction of foreign material into the lungs.

Among the clinical contributors to this subject, Traube, Skoda, Bamberger, and Lebert are particularly worthy of notice. In more recent literature the work of Buhl[3] deserves particular mention. In this spirited and suggestive work, which is, however, marred by too biassed anatomical views, everything is considered which can relate to the subject in hand.

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[1] l. c., p. 107.

[2] Virchow's Archiv, Bd. XIX., S. 103–110, und Virchow's Handbuch der Pathologie, Bd. V., S. 751 ff.

[3] Zwölf Briefe, etc.

Etiology.

Interstitial pneumonia is not to be regarded as an independent disease, but as the result of other morbid processes. Changes in the nutrition of the lung-tissue are necessary for its production.

These two general propositions contain all upon which both anatomists and clinicians are agreed. As soon as we advance any further we find that the two sets of observers begin to differ. The following are the opposing views:

It is possible for an inflammatory excitant, beginning in the bronchi and expending its first force upon the mucous membrane which it finds there, to penetrate to such a depth that if powerful enough it will attack the connective tissue of the lungs and place it in a state of inflammation. A bronchial catarrh supplies this excitant, and is the most common cause of interstitial pneumonia.

The other view is this:

Inflammatory changes only occur in the framework of the lungs as a result of particular conditions of nutrition, which are the expression and result of a peculiar constitutional anomaly. An inflammation of the bronchial mucous membrane is not sufficient to produce them.

It is rather curious, though it may be nothing more than a coincidence, that the representatives of these opposing views should be on the one hand a clinical observer,—namely, Niemeyer,—and on the other, an investigator who seeks his knowledge at the autopsy table, like Buhl.

The picture which anatomy holds up to us shows the thing created, but not the method. And it requires the greatest insight to use this picture correctly for the right interpretation of the relations of pathological changes found lying side by side. Though in a given tissue changes may be found further advanced than those in a neighboring tissue, still how are we to be certain from this that the reaction of these different tissues, to the same morbific agent, though the latter may act upon both simultaneously, is the same in each?

Practically the whole thing amounts to this: that we are compelled to accept as probable the specific relations of certain constituents of the body to certain agents, and it is of little import whether they be introduced from without in a perfect form or whether they be engendered in the body. The action of poisons furnish us with the best proof of this. It seems but justifiable, therefore, to apply a similar process of reasoning to inflammations of the lungs. We should keep in mind, however, that we are acquainted with too few positive facts bearing upon this subject to give a hasty or premature decision.

If the view that tubercular virus is contagious and absorbable by the lungs be correct, (and many hold that it is so), what objection can there be to going a step further and supposing that the virus has a particular affinity for some special part of the lungs, or, at any rate, that it attacks one part with greater avidity than others?

It is certainly just as allowable to advance these and similar hypotheses as it is to suppose certain changes must perforce have travelled in a direction from within outward, or *vice versa*, when the only basis for such a supposition is the fact that a lesion, which, extending through from the surface to deeper parts below it, is found to be more marked in one part of the degenerated site than another.

An anatomist, reasoning in this way, does not present us, as he supposes he does, with the actual facts themselves, but only gives us a clew to what they possibly may be, and the hypotheses which he erects are such as require much weightier proofs before they can be accepted.

When Buhl, therefore, affirms that an ordinary catarrhal bronchitis can never become the cause of interstitial pneumonia, he oversteps the limits which an anatomist's methods of research impose upon him; and certainly none of the proofs advanced by him in support of his opinions are sufficiently conclusive.

"It would be a grave error," he says, "to trace the origin and progress of the inflammatory processes from the bronchial mucous membrane to the pulmonary parenchyma, instead of *vice versa*."[1]

[1] Zwölf Briefe, S. 62.

Similar objections hold good for other statements made by him. As, for instance, where he says: "Even the most tedious catarrh confines itself solely to the mucous membrane, causing only a thickening of the innermost layers of the bronchial wall, and leaving the others, especially the connective-tissue sheath, entirely untouched." [1]

Even Buhl himself, however, cannot always support his views throughout. He is forced to admit that, at times, the irritation arising from decomposing pus and mucus may cause an inflammation of the whole bronchial wall, including its connective-tissue sheath. But by admitting this he in reality admits everything. For there can be no decomposing secretion without a previous bronchial catarrh, and when the question is raised, whether the latter can cause an interstitial pneumonia or not, it is, after all, immaterial whether it occur directly or indirectly.

Those who defend the doctrine advanced by Buhl must, therefore, at least tacitly admit that catarrhs, especially when of long duration, may morbidly influence the parenchyma of the lung. They seem to place, at any rate, considerable importance on "decomposing secretion."

While we have here been criticising, perhaps somewhat severely, the anatomical methods as practised at the autopsy table, it will be only fair to own that the means employed at the bedside are in no way refined enough to give intelligence of changes in the pulmonary framework, especially when these are in their incipiency.

Signs which we recognize in a case of consolidation at the apices may have but one physical meaning, while pathologically their significance may be manifold. The dull sound heard on percussing a spot may be indicative of a diminished quantity of air in that part of the lung; but physical examination by means of percussion cannot tell us whether there is any swelling of the interstitial tissue, or an obstruction of the bronchioles with alveolar collapse, or whether there is an accumulation of pus and mucus in the bronchi, the result of tuberculous processes. The results of auscultation are equally meagre. The only impres-

[1] Op. cit., p. 16.

sions conveyed to our ear are, that air is rushing through a number of irregularly constricted connected tubes, which are filled, perhaps, with a more or less tenacious fluid. How are we to tell whether the constrictions are caused by a thickening of the superficial or the deep layers of the bronchi, or whether the fluid is the result of an irritation of the surface, or whether it has made its way up from the deeper layers of tissue lying below? Who would be bold enough to enter here into any absolute demonstration?

A clinician who, from the results of his first examination, may have diagnosticated a catarrh, and finds later, at the same spot, a consolidation, and then concludes that the consolidation is the result of the previous catarrh, certainly deduces his conclusions by methods not warranted by strict scientific inquiry. He, too, presents but hypotheses,—mere speculations, really, which lack confirmatory proof. And it is just this that Niemeyer and others have done. while they fondly imagined they were giving us actual facts.

The experiment of the inhalation of dust to which many human beings involuntarily subject themselves, and the supplemental experiments performed upon animals, deserve a somewhat extended notice, for from them we may gain a conception which, though it presents, in many respects, but a possibility of what the actual processes are, still bears with it the suggestion of a more thorough penetration into the philosophy of the subject.

These "dust-lungs," as they are called, present one regularly recurring phenomenon; that is, the foreign bodies inhaled are always found in the interstitial tissue.

Investigations pursued by von Ins,[1] under the direction of Langhaus, make it appear that one of the first results of the introduction into the lungs of masses of dust is to cause an immigration of the white blood-globules into the air-cells. These wandering cells absorb the dust, and carry it into the pulmonary framework, partly by way of the lymphatic vessels, and partly by the direct passage of the cells through the tissues. Having

[1] Archiv f. experiment. Pathologie, etc. Bd. V.

once arrived in the connective tissue, the white blood-globules may disappear entirely again by being conducted into the bronchial lymphatic glands, and there remaining. This, however, does not always happen, for should the quantity of dust exceed a certain measure, the cells do not leave the interstitial tissue, but remain stationary in it.

Another fact, the result of clinical observation, is that *large accumulations of dust may occur in the pulmonary stroma, without necessarily exciting inflammatory changes at their sites* (Traube [1] and Cohnheim). This holds true, at least, where coal-dust and the oxide of iron are concerned (Zenker [2]); and von Ins's investigations have proved it so, also, for clay-dust.

Why is it, and what are the circumstances which cause these "dust-lungs" to become the seat of inflammation at one time and not at another? And when inflammation does occur, why is it not equally distributed throughout all parts containing dust? These seeming inconsistencies make it necessary to suppose the presence of some other irritant besides dust to explain all the phenomena which occur. Traube has already called attention to these puzzling questions.

It is possible that such an irritant might be produced in the body chemically from certain kinds of dust that enter it.

This idea has gained favor from the results of some of von Ins's observations. He found that when chalk and clay dusts were inhaled simultaneously by dogs, the former soon disappeared, while the latter remained. The disappearance of the chalk being due, according to his explanation, to the carbonic acid contained in the blood and fluids of the lung-tissue, converting the insoluble carbonate into a soluble bicarbonate of lime.

It is most probable that in the majority of cases the necessary irritant is furnished by the secretion resulting from a bronchial catarrh. This secretion, as we know, either has the property of exciting inflammation inherent in it from the very beginning, or acquires it after exposure to the air.

The question which has been raised, as to whether the phlogistic element resides in the fluid or solid parts of this secretion,

[1] Ges. Abhandlungen. II. Bd. S. 525 and S. 771.

[2] Deutsches Archiv fur klin. Medic. Bd. II. S. 156.

or whether it belongs to its cellular portions, is one which has but little bearing upon the present discussion.

That reabsorption can take place from the bronchial mucous membrane through the blood-vessels and lymphatics certainly needs no confirmation here, and there seems to be no objection either to the idea that in old catarrhs, accompanied by severe coughing, some portions of the bronchial secretion are carried into the alveoli, and there absorbed.

Von Ins's experiments seem to have proved conclusively that the accumulation of large quantities of foreign material in the connective tissue of the lung not only interferes to a marked degree with the movements of the wandering cells (leucocytes), as has been already pointed out, but also presents serious obstructions to the currents of lymph which flow through the lungs. From this it is quite evident *that an inflammatory excitant contained either in the wandering cells or in the lymph, and which in the normal condition of the lungs would remain too short a time to do any mischief, could now, under these conditions, remain long enough in contact with the connective tissue to place it in a state of inflammation.*

It seems to me that the reason why "dust-lungs" are more readily attacked than others by interstitial pneumonia is readily explicable on these grounds.

Besides the above causes, we have the fact that chronic catarrhs of a severe type are the rule in these lungs. So here we have the necessary inflammatory irritant superadded to the "increased predisposition" caused by the deposition of dust.

The reason why these lungs are not inflamed throughout, but are rather the seat of disseminated patches of inflammation, can be explained by the same cause. For the obstructions to the lymph currents are as little equally great in all parts as the bronchial catarrh is equally distributed.

Are those conditions which obtain for the dust-lungs applicable to a simple catarrh? This is a question which may be raised with propriety.

We know from experience that an irritant fitted for the production of inflammation may unfold this property as soon as it operates with sufficient strength, and for a sufficiently long time

upon a tissue capable of being inflamed. The two latter conditions being in so far supplemental, that the result attained by the continuous action of a mild irritant is also produced by the rapid effects of a powerful one.

Why, now, is it not quite possible that *in cases of bronchial catarrh of long duration* the resulting secretion (undergoing decomposition, it is true, as we must admit with Buhl), should not be able, just on account of this chronicity of the disease, to excite an inflammation in the interstitial substance of the lung? The irritation in itself need not amount to much. Its power, at least, would not be so great but that, under ordinary circumstances, the forces determining tissue changes would amply suffice to counteract it. But with a long-continued and constantly renewed irritation, together with a lymph flow, retarded from whatever cause, it seems easy to see what would happen.

It might be well to bear in mind, too, that different catarrhs, though seemingly anatomically identical, furnish secretions varying greatly in their irritant properties. Every physician knows how a bronchitis, once introduced into a family, will attack every member of it, and under circumstances, too, which do not admit of the favorite explanation of "catching cold."

The analogy of a bronchitis to a virulent urethral catarrh presents itself almost involuntarily. Just as a long-continued gonorrhœa causes inflammation of connective tissue and produces cicatricial constrictions, so, too, may a strongly irritating and long-continued bronchial secretion.

Measles, whooping-cough, and putrid bronchitis are diseases in which contractions of the lungs are most frequently seen, and autopsies performed during the height of their catarrhal processes show the bronchial lymphatic glands to be almost always greatly swollen. That these glands have been placed in a state of inflammation by irritants that have passed through them can be as little doubted, I think, as that these irritants were derived from the secretion of the bronchial mucous membrane.

Thus, we see from the above how facts appear from all sides, confirming the probability that the inflammatory changes occurring in the pulmonary stroma are produced by bronchial secretion.

And now, after having considered bronchitis itself, let us take a glance at *catarrhal pneumonia*, which, with a constantly decreasing number of exceptions, arises from bronchitis.

Buhl, it is true, contends that this disease, like the other, seldom leaves anything else behind it but "exceptionally" local emphysema, atelectasis, and bronchioles plugged with mucus.[1] But is it possible that Buhl the clinician can agree with Buhl the anatomist?

Furthermore, *that form of pneumonia which occurs after section of the vagus is a catarrhal one.* Since Traube's demonstration, all are now agreed to this fact. Experimental proofs are not wanting, therefore, to demonstrate that in a catarrhal pneumonia of this kind, running the most rapid course of any, the interstitial tissue of the lungs is by no means unaffected.

Friedlaender says[2] "that in pneumonias, both of the experimental kind and those occurring in children, one never-failing factor is the appearance of numerous lymphoid cells in the interstitial connective tissue and lumina of the alveoli." Von Ins's investigations support these opinions entirely, so that here, too, more weight is added to the evidence against Buhl's assertions. Only by experimental methods, whose results would refute the views of his opposers, could he again strengthen them. Until this be done, pathological research of an experimental kind still confirms the proposition that *catarrh of the bronchi may lead to interstitial pneumonia.*

I have said *bronchi* advisedly, for the intervening factors of catarrhal pneumonia, with, perhaps, an absorption of the irritant from the alveoli alone, are of but subordinate importance here, where it is a question of the origin, the cause of this connective tissue disease.

While the recognition and appreciation of the fact that the peculiar structure of the lung must have considerable influence in determining those changes is one that should not be lost sight

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[1] Zwölf Briefe, S. 21.

[2] Untersuchungen über Lungenentzündung, etc., S. 16, and a further exposition in Virchow's Archiv. Bd. LXVIII. Experimentaluntersuchungen über chronische Pneumonie und Lungenschwindsucht.

of, still it is not right to allow this "predisposition" to assume the importance which Buhl gives to it.

Although he also introduces it under the name of tuberculosis, Buhl makes the disease, which he calls desquamative pneumonia, the sole issue of every morbid process, extending deeply and causing, at the same time, a disturbance of the pulmonary framework. He makes it the dominant factor, too, of all chronic lung diseases connected with inflammation. This certainly is going a little too far.

In confirmation of the above, the following is a quoted paragraph embracing his opinions on this subject:

"*Tuberculous pneumonia, therefore, is nothing but an intensification of genuine desquamative pneumonia.* The latter then comes to be rightly recognized as the expression of a general disease. This general disease belongs to a constitution which, if we were to schematize it according to varying grades of intensity, would at first be content to produce nothing but spindle and star shaped cells as its inflammatory exudation. (This stage may be designated as the true desquamative pneumonia which ends in cirrhosis.) Soon, however, there would be added to these an increase in the number of endothelial cells of the lymphatics (cheesy pneumonia), and in the still higher grades lymphomata (tubercular pneumonia). In the most serious cases, as in purulent peribronchitis with lobular degeneration, infiltration of pus is found."[1]

In this, as in many other diseases, the supposition of a variable power of resistance to morbid influences of the lungs of an individual gives us a welcome explanation why one person suffers oftener, and to a greater degree, from severe disturbances of these organs than another. But further than that it may offer some therapeutic suggestions, this idea is not worthy of any more extended consideration.

In the present state of our knowledge, there can be but little to object to in the proposition that long-continued bronchial catarrhs may produce a proliferation,—i.e., inflammation,—of the connective tissue of the lungs. They may likewise favor, by various means, the formation of bronchiectatic cavities,[2] *whether these are or are not associated with shrinkage of the lung.*

These general propositions which have been laid down are

[1] Zwölf Briefe, S. 135.

[2] See page 859 of this article.

intended to be followed by the discussion of more special ones, and first of all those diseases which occur with interstitial pneumonia will be examined into. In doing this, however, very careful regard should be paid to whether any really fundamental relations exist or not between interstitial pneumonia and the diseases to be considered.

It is of great theoretical, though of little clinical, importance that *syphilis* is capable of producing the disease in question. Virchow, who has given this subject a very careful consideration, thinks the most common pulmonary disease produced by syphilis to be either a chronic multiple pleuropneumonia or a bronchopneumonia.[1]

"On the surface of the organ, either on or immediately beneath the pleura, or situated about the circumference of the bronchi, very dense and distinctly indurated nodules are found. Those situated at the surface of the lung are often of a cicatricial nature, while those in the interior of the organ have an irregular or even markedly knobbed character. They are hard to the feel, are cut with difficulty, and consist of a very firm, often distinctly sclerotic connective tissue, which though in itself perfectly white, frequently assumes a mottled, bluish, or even black appearance, from the absorption of coal-dust. These nodules are often as large as a walnut, and when there are a number of them lying close together, a large part of the lung may be rendered practically useless and the patient become asthmatic. It is not infrequent, furthermore, to find places in them which, though yellow, are not distinctly caseous. Microscopical examination of these yellow spots shows in them the presence of an incomplete fatty metamorphosis, be it of the connective tissue proper or of the cells newly formed from the latter. It is evident that a marked resemblance exists here to the gummata of the periosteum and of the liver. It is highly probable, too, that later on a reabsorption of the fat takes place.[2]

Virchow adds also that he was unable to detect any anatomically specific difference between the pneumonia of syphilis and that afflicting grinders and polishers—that is, of a dust disease.[3]

In the various forms of *pulmonary phthisis*, aside from the absence or presence of tuberculosis, interstitial pneumonia plays a conspicuous part. It is even present, according to Rindfleisch,

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[1] Geschwulstlehre II., S. 466. [2] Virchow, loc. cit.

[3] Consult the article by *Baeumler* in Vol. III. of this Cyclopædia.

in lungs which are the seat of acute miliary tuberculosis. But this condition has been so thoroughly treated of in another part of this work that I cannot do better than refer the reader to it.

The relation of interstitial pneumonia to *diseases produced by the inhalation of dust*, have already been treated of, and the significance of *bronchial catarrhs* in the production of this disease have likewise been explained.

The further a catarrh extends into the smaller bronchi, and the longer it lasts, the more probable does it become that the interstitial lung tissue will become involved in the inflammatory processes going on. It is very likely, however, that in the majority of cases an intermediate step between the bronchial inflammation and that of the connective tissue is necessary, and this is, namely, disease of the alveoli which in itself is a result of bronchitis. My experience has been, that extensive catarrhal pneumonias of the lower lobes, after healing nearly always give rise to a more or less extensive contraction, and to a devastation of the lung, such as is seldom seen more strongly marked even after a long-continued pleurisy.

In the course of time, *tuberculosis* may occasionally appear in an interstitial pneumonia of the latter type, its appearance or non-appearance being often determined by a caseous deposit remaining anywhere in the body from which infection may proceed. Such a cheesy focus is not infrequently produced by a capillary bronchitis and the catarrhal pneumonia attending it, occurring at the same time that the pneumonia does. The bronchial lymphatic glands are its most common seat.

The changes mentioned above, namely, contraction and consequent practical uselessness of the lung, may exist many years and remain entirely free from tuberculosis, or they may even be the seat of a mild form of this disease, without its ever involving extensive areas, or developing into a severer form.[1]

Among the acute infectious diseases, *whooping-cough* and *measles* are those which most frequently leave pulmonary cirrhosis behind them. The extensive bronchitis which always accompanies them being a sufficient explanation for this.

[1] See farther on, p. 859 et seq.

Following these diseases comes *typhoid fever*. It is true, that with physicians who understand the treatment of the disease, this complication is less frequent than it used to be. The catarrh of the smaller bronchi which occurs in typhoid fever may lead to pulmonary collapse, and so to catarrhal pneumonia. The hypostatic congestion too, caused by an insufficient heart's action, contributes largely to its formation. But here, as in the other cases, catarrhal bronchitis is after all the original cause.

In order that the statement just made regarding the preventability of bronchitis in typhoid fever may not stand without confirmation, I would remark that in one hundred and fifty-four cases of this disease, reported in my monograph,[1] but twelve presented any signs of consolidation of the lungs during the course of the disease, and these only for a short time.

In one hundred and eighteen autopsies made on the bodies of patients who had died of typhoid fever, Griesinger[2] found, by personal observation, hypostatic pneumonia in thirty-two—being somewhat more than twenty-seven per cent. of the whole. Murchison[3] found it seven times in nineteen cases, and Louis, according to the former, nineteen times in forty-six cases.

On the other hand, of two hundred and fifty cases examined post-mortem by Hoffmann,[4] and which were taken from Liebermeister's hospital division during the Basle epidemic, but thirty-five had hypostatic pneumonia—that is fourteen per cent. of the whole, which is just one-half less than that excellent physician Griesinger had, who treated his cases according to a more antiquated method.

After *croupous pneumonia*, the interstitial variety is not very common, but that it may develop, any physician of experience can testify.[5]

Extensive *pleuritic effusions* which have existed for some time, not uncommonly leave behind them a lung which has suffered to a very great degree from extensive proliferation of its connective tissue. After trivial pleural irritations, such as only result in a slight thickening and opacity, the interstitial pneumonia, which is rarely absent, confines itself to the immediate

[1] Klin. Studien über die Behandlung des Abdominaltyphus, S. 108.

[2] Infectionskrankheiten. Erlangen, Enke, II. Aufl., S. 207.

[3] Die typhoiden Krankheiten. Braunschweig, Vieweg, S. 570.

[4] Untersuchungen über die pathol.-anatom. Veränderungen der Organe bei dem Abdominaltyphus. Leipzig, Vogel. S. 261.

[5] See in Vol. V. the account of the pathological anatomy in the article on Croupous Pneumonia.

neighborhood of the pleural inflammation, and in many cases is only discoverable on close investigation. If it is allowable to judge of the intensity of an inflammation by its products—a proceeding the propriety of which few would deny, we may say, generally, that the stronger the inflammatory irritation, which acted upon the pleura, the greater will be the probability that if long enough continued, it will react upon the lung itself.

Hemorrhagic pleural effusions, when not traumatic, are generally of too short duration to be of effect, occurring as they do in rapidly fatal diseases (tuberculosis, severe acute infectious diseases, etc.).

Purulent effusions—the next step in a descending grade—after disappearing, invariably leave a shrunken lung behind them.

After a *serous exudation* the lung is usually but little affected.

Finally, to complete the subject, it is worthy of notice that foreign bodies—aside from dust—such as neoplasms, hemorrhages into the parenchyma, etc., cause an inflammation of the connective tissue, which results in their encapsulation.

From the fact that interstitial pneumonic processes and the diseases just mentioned are found in such close contiguity to one another, are we justified in ascribing to them a causative connection?

Interstitial pneumonia certainly presupposes as necessary for its production some inflammatory change in the lungs, and this, in its turn, demands an inflammatory excitant. As soon as the existence of the latter, and the possibility of its reaching a morbid spot in the lungs is proved, any systematic enumeration of causes, which at best is necessarily incomplete, is rendered unnecessary.

Phthisis, bronchial catarrhs, foreign bodies invading the lungs, and pneumonias which always leave diseases of the bronchi connected with them, may be regarded as possessing irritants adaptable for producing the disease in question, and the channels for their absorption into the framework of the lung are always open.

In pleurisy the same thing obtains. Cells, having the property of independent motion, penetrate the pleural surface of the

lung, just as readily as fluids. And it seems impossible that the lung should not be affected, when the circulatory channels of the pleura,—*i.e.*, the bronchial vessels—are the same as those which supply those parts of the lungs not fed by the pulmonary vessels proper. The lymphatics of the lungs and the pleura, too, are both directed toward a common destination.

It would seem for the present, therefore, as if there were no good reason for supposing a merely accidental connection between interstitial pneumonia and the diseases discussed above. On the contrary, their very frequent coincident occurrence points to one common cause. This pneumonia, however, is not always associated with these primary affections, but only exceptionally, —sometimes more, sometimes less frequently. Other causes, therefore, must be at work. What these causes are is a question yet to be solved.

However much bronchiectasis and interstitial pneumonia may be related, their separate identities, nevertheless, should always be carefully preserved. In order, therefore, to come most quickly to a clear understanding of the subject let us now take up the causes of the formation of brochiectatic cavities and investigate their nature.

In this investigation I shall follow Biermer, who presents the existing conditions with great clearness.

Bronchi, even in their normal condition, are subjected to the pressure exerted by a column of air set in motion by the respiratory muscles,—nevertheless, under ordinary circumstances, no dilatations occur in them. In order to produce dilatation it is necessary that either or both of two things should happen, namely, either *the propelling force must be augmented*, together with a local increase of the number of points to be attacked, or *the resistance presented to dilatation must become less.*

Let us consider each of these conditions separately.

Augmentation of the Propelling Force.—During the violent expiration which occurs in coughing, an act aided by intermittent momentary closures of the glottis, the air is driven from the lungs with a correspondingly intermittent force and a very considerable increase in the intrapulmonary pressure takes place. This pressure alone, however, would never be sufficient to per-

manently stretch normally constituted and well-nourished bronchi, nor would any degree of deep inspiration effect it. We must, therefore, seek elsewhere for causes. These will be found in the disturbances which old pleuritic adhesions create in the lungs. For when localized adhesions impede the free movements of the lungs enough to prevent the latter from following the descending inspiratory or ascending expiratory motions of the thorax, the interference thus presented compels the power which this respiratory motion otherwise exerts to expend itself on parts lying in the neighborhood of the adhesions. The same thing is found to obtain where either single bronchi or groups of alveoli have become impermeable.

In these cases, therefore, it is an obstruction to the entering current of air which becomes the cause of the dilatation of those bronchi leading to the adherent portions of the lung.

Diminished Resistance.—This may be caused either by an original defect in the lungs or by some subsequently acquired weakness. The latter condition occurs in senility, where the bronchi, together with all the other organs, partake of a generally lessened nutrition of their tissues. Inflammatory changes afford another cause, for whether they occur in the bronchial mucous membrane or arise from more deeply lying tissues, they create a condition of enfeebled resistance by decreasing the elasticity of the bronchi and paralyzing their intrinsic muscles.

Contractions of cicatricial connective tissue in the lungs exert, according to Corrigan, a very marked dilating force upon the bronchi. This force may act either indirectly or directly: indirectly, by destruction of the parenchyma lying about certain bronchial ramifications and a consequent occurrence of dilatation of these bronchi by respiratory pressure; or directly, by the contraction of the newly proliferated connective tissue enveloping the bronchi, subjecting the latter, already weakened by the same inflammatory processes which have caused the proliferation, to a more or less powerful dilating strain.

Biermer accepts this view, especially for those cases where bronchial dilatations exist in the midst of indurated tissue without extending beyond it. Ruehle, too, gives his support to this explanation. No apology is needed if attention be

again called to the fact that Corrigan by no means insists upon cicatricial contraction as the sole dilating agent, but, on the contrary, he lays especial stress upon the compensatory, space-filling causative element.[1]

Biermer rejects, on seemingly very good grounds, Laennec's idea that the pressure of retained bronchial secretion may produce dilatation.

The following are his objections:

1. The pressure of the accumulated secretion is too trivial to overcome the resistance offered by the bronchus.
2. Retention of secretion is as often present without bronchiectasis as
3. Bronchiectasis is without retention of secretion.
4. Retention of secretion is either a result of bronchiectasis or is, at least, a coefficient of those causes determining bronchiectasis.

According to Biermer's views interstitial pneumonia would afford abundant cause for bronchiectasis, for the inflammatory swelling of the connective tissue of the lungs must diminish their elasticity and power of resistance, just as it paralyzes the contractility of the bronchial muscles. Furthermore, by closing various bronchi in different parts of the lungs, the inflammatory processes which still go on serve to increase the number of points for the respiratory muscles to act upon.

In view of the above well-proven points it would certainly seem to be taking too restricted a view of the subject to consider cicatricial contraction as the sole factor concerned in the production of bronchiectasis.

The most important questions which we have to deal with in this connection are certainly the following:

To what amount is interstitial pneumonia developed about bronchiectatic cavities, and is it of invariable occurrence? Can it be shown whether it existed prior to the disease of the bronchi, simultaneously with it, or whether it was of later appearance?

Biermer, depending for his opinions on a large number of personal observations, expresses himself, in connection with the above, as follows:[2]

In lungs the seat of bronchiectasis, there is not infrequently no disease of the alveolar tissue, though in the neighborhood of

[1] See p. 843 of this article.

[2] Virchow's Archiv, Bd. XIX., S. 153.

dilatations this tissue is frequently flabby and shrunken, and even, in places, emphysematous. These changes in the parenchyma are the result of bronchial disease.

Sometimes inflammatory changes and interstitial pneumonia precede bronchiectasis. In these cases the dilatations are, as a rule, secondary.

On the other hand, proliferation of the connective tissue, with contraction, may be associated with bronchiectasis.

Lebert takes even a more radical view than Biermer. According to him, "*the influence which inflammation of the connective tissue has upon the muscular and elastic elements of the bronchi is the original cause of bronchial dilatations. All other pathological factors have merely a favoring influence upon this condition.*" [1]

But if Biermer, in his investigations, found bronchial dilatations, (often even those of marked size), without interstitial pneumonia, Lebert's statements must be regarded as disproven.

We have now seen, therefore, how the theory of bronchiectasis cannot be made to merge and disappear into that of interstitial pneumonia, but how each, on the contrary, must be kept separate and distinct.

To enumerate the diseases which may be followed by bronchiectasis will be unnecessary, for it would be but a mere repetition of those mentioned as causing interstitial pneumonia. Suffice it to say that here again, however, bronchial catarrh is of the first importance, pleurisy being next.

It is very common to find diseases of the pleura associated with bronchiectasis. In thirty accurately observed cases Barth found but four without old pleuritic affections. Biermer calls attention to the fact that, in the eighteen cases out of fifty-four examined by him, which did not have any disease of the lung proper, all had old pleurisy, and in only eight cases was the latter completely absent. As a rule, bronchial dilatations were most marked in those cases where, as a result of contractions, great deformity of the lung existed.

Biermer considers that, in all his cases where there was no

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[1] Klinik der Brustkrankheiten, Bd. I., S. 312.

previous lung disease, the pleurisy either pre-existed or accompanied the bronchial dilatations. Only in exceptional cases was the opposite probable.

Clinical observations seem to prove the same thing. In patients suffering with bronchiectasis recent pleurisies are rare, and effusions still more so. There is nothing in bronchiectasis, therefore, favoring pleurisy, as at first it seemed there might be.

Lebert, too, ascribes much importance to pleurisy. He thinks that it not only promotes bronchiectasis mechanically, but may also be a starting-point for interstitial pneumonia. He explains the latter by a process already alluded to, namely, that the inflammatory irritant, proceeding from the deeper layers of the pleura to those portions of the lung nourished by the same vessels (the bronchial arteries), effects the same here that it did in the pleura.[1]

Comparative data of certain extrinsic factors affecting bronchiectasis have been compiled at various times. These, it is true, are hardly of much importance, as we have not an autonomous disease to deal with. In these compilations only those forms have been considered which, clinically, it is customary to regard as independent. Tuberculosis has been admitted only in those cases when it was supposed to be complicated with bronchiectasis. Trojanowsky has collected seventy-seven cases from literary sources, and presented them in a carefully written dissertation.[2] Lebert reports forty-five personal observations, which, however, he has not always accompanied with as full particulars as might be desired.

Combining the information derived from these two sources, we get the following:

Age.—In 113 cases:

18	cases,	or	16	per	cent.	of	the	whole,	occurred	between the ages of 0 and 20.
49	"	"	43	"		"		"	"	20 " 40.
37	"	"	33	"		"		"	"	40 " 60.
9	"	"	8	"		"		beyond the age of 60.		

[1] Loc. cit., p. 303.

[2] Klin. Beiträge zur Lehre von der Bronchiectasie. Dorpat. Dissert. X. 1864.

Sex.—In 113 cases, seventy-one were men and forty-three were women; that is, a ratio of sixty-three per cent. to thirty-seven per cent., or nearly five men to three women.

Environment and Occupation.

Those occupations in which bronchial catarrhs readily occur are, as it might be supposed, those also in which bronchiectasis occurs.

A really satisfactory enumeration, however, is not possible here. Besides, the statistics just quoted are based on too few cases, and are altogether too much the subject of chance to be of great value. I should hardly like to indorse the more than bold conclusions of Lebert.[1]

Pathological Anatomy.

Uncomplicated examples of interstitial pneumonia can hardly occur. What we see in a lung consists generally of changes in the connective-tissue framework, dilatations of the bronchi, and disease of their mucous membrane, and, finally, more or less intensely marked degenerations of the pleura.

A lung presenting all these morbid conditions appears smaller than normal, and is connected to its surroundings by firm adhesions. On removing it from the chest we find that it is enveloped in a pleural membrane several millimetres thick. This is a hard cicatricial mass, cut with difficulty, and poorly supplied with blood-vessels. It is of a white color, except where stained by deposits of pigment, and often shows the impressions of the ribs. From the pleural envelope white or whitish gray bands of connective tissue enter the lung, and are so arranged as to correspond with the lobular structure of the organ. Sometimes these bands are deeply pigmented, being dark gray, or even completely black. The portion of lung between them contains less air than normal, and is pale-looking from containing a diminished amount of blood.

The supplying bronchi appear in various grades of dilatation. Sometimes they are everywhere equally enlarged, and at other

[1] Loc. cit., p. 307.

times constrictions alternate with dilatations in regular succession. In other regions of the lung we find bronchi which, dilated from their origin, have been gradually converted into empty hollow chambers as they proceeded. Or we notice how a number of irregularly formed, strangely distorted tubes will start from a main trunk, and, traversing the lung, leave but little of its original structure behind. At other times there is a tangled system of tubes, which may assume a circular arrangement, or, spreading diffusely, traverse a great part of the lung.

The mucous membrane of the bronchi leading to the affected portion of lung is in a state of catarrhal inflammation. It is swollen, markedly injected, and covered with a tough yellow or yellowish green mucus, or, it may be, with an offensive secretion in a state of cheesy degeneration. In the larger cavities the contents are frequently putrid, and emit a horrible stench. The pulmonary arteries are sometimes dilated; they may be the seat of a fatty or atheromatous degeneration, or of thrombosis.

In other cases the lung is markedly emphysematous. Scattered throughout are bronchial dilatations, in whose surroundings the lung-tissue appears wasted, collapsed, and infiltrated with œdematous fluid, or destroyed by cicatricial shrinkage.

Again, instead of the greater part or whole of the lung, one lobe only may be seriously affected, the others being simply involved compensatorily.

But it is hardly possible to give a general description which shall embrace every circumstance occurring. It will, therefore, be better to take up each pathological condition in detail.

The Forms of Bronchial Dilatations.—Laennec was the first to distinguish between uniform (cylindrical) and saccular dilatations. He was followed by others, especially by Rokitansky and Biermer.

In *uniform dilatations*, the bronchus at a certain point in its course undergoes an increase in its circumference, which may persist for some distance. This increase may be so considerable that branches, which in their normal state would hardly admit a probe, may now become large enough to admit a quill, or even a finger (Laennec). In this way branches so enlarged may surpass in size the trunk from which they originally sprang.

Very frequently an extensive division of the bronchial tree is the seat of this form of cylindrical dilatation, so that all parts of the particular division involved become equably affected. That is to say, all the relations of the bronchi to each other in point of size are retained, but there is a general increase of them all. On the other hand, a dilatation increasing as we near the peripheral bronchioles may occur. According to Rokitansky, this is more common.

Subordinate varieties of the uniform variety of dilatation are those confined to a limited length of the bronchus, and which are called *spindle-shaped*, and those in which dilatations are interrupted by normal sections like beads on a string. These latter are called *moniliform*. The latter kind is most frequently seen in medium-sized bronchi. After severe catarrhs of the capillary bronchi, especially in children, cylindrical dilatation, which usually affects anyhow only the peripheral distribution of the bronchial tubes, is likely to occur.

In *saccular dilatations* the bronchial tube is expanded into a hollow space, which is generally of a more or less spheroidal shape. Usually the dilatation preponderates more in one direction than in another. It may take place in two ways, either in continuity, so that the points of entrance and exit remain of their normal size, or a bronchus, beginning to dilate at a certain point, may continue to do so to its end, being thus gradually converted into a single large chamber. Another possible occurrence that may arise is the involvement of a large division of bronchial ramifications. In this latter case, numerous sacs of every size are so closely crowded together that they really form but one large cavity, the latter it is true having numerous pouches and recesses, which are separated from each other by valvular and band-like reduplications of the bronchial walls. According to Reynaud, Rokitansky, and Biermer, saccular dilatation is most likely to occur in the neighborhood of bronchial stenoses.

As a rule, *in saccular dilatation, only one opening leading into a bronchial tube can be found;* and it may even occur, that by occlusion or obliteration of this opening, the bronchiectatic cavity becomes entirely isolated (Biermer).

Saccular dilatation, too, occurs as a rule only in the middle-

sized or smaller bronchi, and only under very exceptional circumstances are the larger branches the seat of this change. The cavities themselves vary from the size of a pea to that of a hen's egg.

The two forms are generally combined, and their frequent and, indeed, almost invariable occurrence together in the same bronchus, would prove that there is really no essential difference between the two. It is only for the sake of convenience, and in order to systematize the subject, that we have arranged them into two kinds (Biermer, Lebert).

The walls of the bronchiectases present a very variable appearance, a fact to which Laennec already directed attention. He, and at a later date, Rokitansky, were content to say that sometimes hypertrophy and sometimes atrophy were present. Biermer, on the other hand, not satisfied with this, divided the changes found into the following types :[1]

1. *Dilatations in which the bronchial walls are in a state of simple catarrhal swelling and relaxation depending on an acute inflammation.*

This condition is found most usually in the lungs of children having bronchitis. A complete recovery is possible.

2. *Dilatations having hypertrophied walls.*

The bronchial mucous membrane is distinctly thickened and usually much congested. The submucous connective tissue is generally involved as well in this process of thickening. Atrophy is usually absent in this variety. Bronchi of large or middle-sized calibres, with cylindrical or spindle-shaped dilatations, usually present this form. The hypertrophy of the mucous membrane is generally not continued beyond the seat of disease.

3. *Dilatations with atrophied walls.*

In these the atrophy may be absolute or it may only be relative. In the first case the bronchial walls are reduced to a thin layer of mucous membrane, while in the latter they only appear thin in comparison with the space which they enclose. The atrophic form is the rule in saccular dilatation, but it is also found in the cylindrical dilatations of the bronchioles.

4. *Dilatations with trabecular degeneration of the walls.*

[1] The following is for the most part in Biermer's own language.

In this form the walls of the bronchiectatic cavities are no longer smooth, but are the seat of depressions and elevations, the former being caused by local atrophies and the latter by the persistence of remaining circular and longitudinal fibres. There is, therefore, a mixed condition of atrophy and hypertrophy present.

Various secondary changes may appear in dilatations after they have been completely formed, and among these is ulceration. This may occur in several ways. The retained and decomposing secretion erodes the walls of the dilatation, and thus leads to the formation of an ulcer, or the contraction of the cicatricial tissue about the dilatation compresses the nutrient vessels, and the bronchial wall, thus deprived of nutrition, dies, and in so doing subjects itself to all the chemical irritants engendered by its decomposition. In these ulcerative processes the absence or presence of organic causes of putrefaction, and the power of resistance shown by the neighboring tissues, have much to do in determining whether the inflammatory processes are to remain of a simple kind, or whether they are to be accompanied by decomposition, and whether they are to extend over a greater or less area.

A hard cicatricial tissue offers a certain amount of protection to the surrounding parts. An œdematous tissue offers less, and one the seat of cheesy or tubercular degeneration the least. It is not uncommon to find that these ulcers have healed.

The points of differential diagnosis existing between ulcerated bronchiectatic cavities and phthisical ones have been described by Virchow.[1] In bronchiectasis the mucous membrane, although much changed in its histological nature, can still be traced over the whole wall of the bronchial dilatation, and is only completely destroyed at certain points, namely, those which are the seat of ulceration. In the walls of tubercular cavities, numerous blood-vessels, either the seat of a thrombosis or entirely obliterated, are found.

Distortions and deformities of bronchiectatic cavities, as the result of an amalgamation of their walls, are not common. On

[1] Verhandlung der physikalisch-medicinischen Gesellschaft in Würzburg. Zweiter Band, 1852, S. 24 ff.

the other hand, it is quite frequent to find them traversed by fibrous bands. This condition has been described by Biermer.

Calcareous degeneration has only been observed a few times.

Attention has already been called to the fact that a bronchiectatic cavity may have all communication with the neighboring tissues cut off and be converted into a cyst by the occlusion of the bronchus from which it was originally formed. The further changes which it undergoes do not differ from those which take place in cysts generally. An inspissation and even calcification of the contents may occur, or the latter may consist simply of serum. This takes place when, from pressure exerted by the encysted fluid, the secreting elements of the cyst-wall have been destroyed, but the blood-vessels have remained intact.

The bronchial mucous membrane[1] is nearly always in a state of catarrhal inflammation, not alone in the dilated bronchi, but also in those of normal size. This catarrh is not infrequently accompanied by considerable hyperæmia, though in the saccular dilatations it is more common to find an anæmic condition of the mucous membrane.

Microscopical examination of the mucous membrane shows the capillaries to be elongated and thrown into small papillary loops, the latter corresponding to minute elevations seen upon the surface. These elevations may be so numerous as to give to the mucous membrane a distinctly villous or shaggy appearance. Where more sparingly distributed, it can be observed that they are arranged parallel to the longitudinal axis of the bronchus in which they may be situated. The papillæ themselves are pyramidal or club-shaped, and always appear very much injected. The capillary loop is covered with a thin homogeneous membrane, provided with numerous layers consisting usually of ciliated epithelia, mingled with round and spindle-shaped intermediary varieties of cells. The ciliated epithelia are always well preserved, and show no deviation from the normal. There is a thickening of the whole bronchial wall. The blood-vessels of the deeper layers are enlarged, and the mucous glands, without

[1] Described by Biermer in Virchow's Archiv, Vol. XIX. Compare also an article by Fitz, "Beitrag zur feineren Anatomie der Bronchiectasie," in Virchow's Archives, Vol. LI.

being actually hypertrophied, are generally abnormally well developed. No special changes have been noted in the muscles and nerves.

The changes just described apply mostly to those forms of bronchiectases in which hypertrophic alterations have taken place. After having persisted for some time, however, the changes are of a far more marked and serious character.

A part of the capillary system, and the remaining elements of the mucous membrane waste away, the longitudinal fibres especially being attacked with this form of atrophy, and the mucous membrane becomes pale.

If the hypertrophic process persists for some considerable period of time, the bronchial cartilages and the connective tissue of the deep layers will also be attacked. Both increase in volume, but the latter, after a while, shrinks, thereby affecting the alveolar portion of the lung lying in its neighborhood.

The minute changes occurring in the cartilages have been exhaustively described by Fitz.

In trabecular degeneration the bronchial wall is, on the whole, thicker than normal. It is the connective-tissue sheath of the bronchus and its cartilages, however, which is increased in volume, for the mucous membrane and muscular elements are generally the seat of atrophy. The mucous membrane nevertheless is usually not very much damaged, for the projections and trabeculæ are always covered with a membrane in which the ciliated epithelium is always well preserved. The trabeculæ are composed of elastic and inelastic connective tissue. Where the degeneration is far advanced, the muscular fibres, which are at best few in numbers, disappear entirely.

Situation of Bronchiectases.—We have two sources of authority on this subject. One, emanating from Trojanowsky, who records seventy-four cases; another from Lebert, who records fifty-four. Although some of the same cases are included in both accounts, we may conclude from both that bronchiectasis is more commonly confined to one lung. Trojanowsky found it thirty-nine times on one side only, and thirty-five times on both sides together. Lebert found it twenty-eight times confined to one lung, and twenty-six times involving both.

Trojanowsky found it occurring in the upper lobes alone fourteen times, against twelve times in the lower. When bronchiectasis occurs on both sides, this author found it to be more marked on one side than on the other; at least in thirty-five cases this occurred twenty-one times. Lebert, on the contrary, found in twenty-six cases that both lungs were equally affected in fifteen of them.

Bronchiectasis less frequently attacks both upper lobes at the same time than both lower lobes. This, at least, was found to be the case by Trojanowsky in eighteen cases for the latter, against four for the former. The left lung is more frequently attacked than the right.

Changes in the pulmonary parenchyma have already been alluded to. Collapse, with an accompanying catarrhal pneumonia, œdema, and a more or less extensive proliferation of the connective tissue, followed by shrinking and pigmentation, are conditions commonly found. In many cases, indeed, a true tuberculosis may occur, or the lung either in the immediate neighborhood of the diseased portion, or in more remote parts, may be the seat of emphysema.

The secretion contained in the bronchiectatic cavities may be carried by the air entering the lungs, into remote parts of these organs, and there set up either simple inflammatory or putrefactive changes. These two conditions, indeed, not infrequently exist side by side; a simple catarrhal pneumonia, often of considerable extent, having true putrefactive foci in its immediate vicinity.

The bronchial lymphatic glands are always more or less involved, being usually enlarged, pigmented, and often, to a great degree, indurated. They may also be the seat of a calcareous deposit or of cheesy foci.

Pleurisy, which is an almost invariable accompaniment, has been described already.

In consequence of contractions in the lungs and of bronchiectases, changes occur in other organs besides those immediately involved. Any marked shrinkage of the lungs occurring in a still yielding thorax causes the latter to sink in, and, as a

consequence, the vertebral column becomes crooked, and the scapulæ project; in fact, there is a condition of kyphoskoliosis.

After the changes in the lung have persisted for some length of time, the heart becomes secondarily involved. Usually the first thing that occurs is an hypertrophy of the right side, accompanied by a more or less marked dilatation. Later, an albuminous or fatty degeneration occurs, giving rise to some cardiac insufficiency, in addition to which a functional or organic valvular disease may be added. Not infrequently atheroma and fatty degeneration of the pulmonary artery are found.

The *liver* and *spleen* show the results of continued congestion by an increase of their connective tissue. In rare cases they may be the seat of amyloid degeneration. A fatty infiltration of the liver, however, is very common.

Occasionally the *kidneys* are the seat of a cyanotic induration, such as is usually caused by venous congestion. This condition, however, is by no means a common one. Amyloid degeneration is still more rarely met with.

In a number of cases the appearance of *general ascites* is either the forerunner of final dissolution or it may be its immediate cause.

Morbid conditions of the *alimentary canal*, except those resulting from œdemas and catarrhs of its mucous membrane, may be regarded more as accidental complications than as direct results of the conditions existing in the lungs.

Pathology.

In order that the morbid conditions here described may not be too narrowly confined or surrounded by the unyielding trammels of system, it is essential to use a freedom which can be dispensed with when giving descriptions of better defined diseases.

Each attempt to draw the lines closer will fail, on account of the many intermediate links—there being a group of anatomical changes which must be considered as a whole, and cannot be dealt with in any part.

We may make a more *anatomical* division, which can be carried out, even during life, by the aid of physical diagnosis: re-

traction with emphysema and bronchial catarrh ; retraction with a great amount of thickening, and retraction with the formation of cavities, would then be separated from one another.

Or, the *clinical history* may be taken as the starting-point ; and in this event we would divide the affection into :

1. Bronchitis, with more or less extensive retraction and emphysema.

2. Different forms which are somewhat similar to phthisis, but differ from it in having more the character of a chronic pneumonia.

3. Dilatation of the bronchi, with the constant or occasional appearance of putrid matter in the expectoration.

Both classifications correspond in the main. I think it best, however, to select the clinical, though I must again remark that a strict separation is hardly possible, and that one is adopted by me as a matter of necessity.

General Clinical History.

The patient generally shows tolerable, very seldom good, *nutrition.* Occasionally, however, obesity exists, and a relatively good muscular development remains. As the disease progresses emaciation takes place, which cannot be relieved, notwithstanding the fact that the patient is placed amid more favorable surroundings.

The physical *powers of endurance* are lessened to a certain extent, though, as a rule, only in one direction. Up to a certain point the patient's ability to accomplish a given work may compare favorably with that of a healthy individual.

Cyanosis exists in all serious changes in the lungs ; in severe bronchiectasis and retraction, the cyanotic condition is sometimes very marked. The face then becomes puffy, and is traversed by enlarged venous radicles ; the tips of the fingers are club-shaped.

The number of *respirations*, when the patient is at rest, is but slightly increased, or normal. It is, however, considerably increased by exertion, and this frequency is occasionally carried to such an extent as to compel cessation of exertion on account of

the want of air. At the same time the *heart's action* is generally not quickened in like proportion—the frequency of the pulse increases much more slowly, although, perhaps, the heart's action becomes stronger. At least, this is the case so long as the heart-muscle remains in good condition, and has not suffered in any degree from degeneration. When this has occurred, increased action always causes failure of the heart.

Fever is always absent; when present it indicates that a complication has supervened.

Cough with expectoration is constantly present, but the character of both changes frequently within broad limits. A symptom peculiar to all these affections remains to be mentioned, viz., that the cough always comes on *in the morning* soon after the patient awakes. It then takes a certain time for the expulsion of the mucus which has collected during the night, and the coughing spells necessary for this purpose are usually somewhat spasmodic. When the accumulated material is removed the patient feels relieved, respiration is easier, and there is freedom from the sensation of oppression and tension of the chest.

The *repetition* of this process of clearing the bronchial tubes, and its relative frequency, depend, apart from the individual surroundings, upon the extent and character of the changes in the lungs, and also in a high degree upon the manner of living. Continuous speaking, the inhalation of dust or other irritants, in short, anything which can contribute to the irritation of the mucous membrane of the bronchial tubes, will bring on augmented secretion. *The character of the expectoration* is so variable that its description will follow with more propriety when we discuss the symptoms of the different forms of the disease. We must mention that hemorrhage of the lungs often occurs in patients suffering from interstitial pneumonia.

We will mention the *physical signs* in considering the special forms of the disease.

The *other organs* show no special abnormal changes connected with this disease.

Although aggravated now and then by a fresh catarrh, and although life is possibly endangered by violent hemorrhage or putrid bronchitis, yet the affection may be prolonged over a pe-

riod of ten years or more. Still the patient's condition rarely remains unchanged during this time. Acute catarrhs—which always occur in the course of the disease—produce pathological changes in hitherto sound parts, cause emphysema, and, finally, progressive degeneration of the heart.

Perfect recovery never occurs; very mild forms may remain free of symptoms.

Death may be brought about in different ways.

The most common cause of *death* is insufficiency of the heart combined with a general dropsical condition and violent dyspnœa.

Slow in its increase, the disease may appear to be checked, but is again brought to a full height by a fresh bronchitis; again, its activity diminishing, the patient may appear to improve. The cardiac affection may permit the patient to live for a number of years; nevertheless, the patient's condition grows continually worse. Finally, emboli form in the lungs, or (more often) thrombi in the pulmonary arteries, and, in a fresh attack, the patient, whose respiratory surface is gradually being sacrificed more and more, and whose cardiac energy is diminishing, finally succumbs. At the post-mortem examination it will be a matter for surprise that so small an unimpaired lung surface, and a heart so far advanced in degeneration, could have sustained life for such a length of time.

At other times, death is due to the *putrid decomposition of the bronchial secretion.*

Putrid bronchitis, with its sequelæ—locally, catarrho-pneumonic spots which are soon involved in the gangrenous process; generally, febrile symptoms of a septic character—will give rise to death within a few days or weeks.

Then, again, the clinical history of consumption may develop: large catarrho-pneumonic caseous masses, rapid breaking down and formation of cavities, sometimes with the development of tubercle, and this associated with hectic fever—presenting all the appearances of phthisis in a rapid or more chronic form.

More rarely death occurs suddenly from the *rupture of a large vessel* in one of the cavities, followed by a violent hemorrhage. Death from pneumothorax is quite a phenomenal occur-

rence. Biermer noticed cases of death caused by *metastatic abscess of the brain.*

The most common *intercurrent acute disease* is *croupous pneumonia.* According to some writers on bronchiectasis it does not often produce death. Croupous pneumonia must, however, greatly endanger the life of these patients whose heart and lungs are both affected.

Following these preliminary observations we will now direct our attention to the consideration of the individual forms and to a few specially important symptoms.

Bronchitis with more or less retraction associated with emphysema.

The diagnostic point in the differentiation of this from other forms depends upon the physical signs and the history of the origin and progress of the disease.

It is not always easy to distinguish it from emphysema. The latter is never absent, nor can we state in each case its physiological significance. If we take into consideration that both conditions are very often produced by the same cause (bronchial catarrh), have originated at the same time, and that severe emphysema is always combined with a certain amount of dilatation of the bronchi, that the diminution of the respiratory surface, in consequence of the destruction of the capillaries of the lungs, occurs in both,—it is clear that physical examination can alone determine whether the emphysema is associated with dilatation of the bronchi or with spots of infiltration. And yet it is precisely this emphysema which makes the physical exploration difficult.

If the disease has developed in childhood, we generally learn that *measles*, or *whooping-cough*, with *pneumonia of long duration*, has preceded it. More rarely, we are told that the child has been coughing for a long time, and that after a pneumonia the disease has changed for the worse.

I do not hesitate to say that a *catarrhal pneumonia* is the most frequent cause of the disease, as, after the epidemic of measles in 1874, I had the opportunity to observe several (five) children for a long period, and in all of the cases the disease developed under observation. It may be considered an advantage for a physician to be located in a small city, for with a little exertion he may easily study the development of a disease.

When the disease sets in at an advanced age a *chronic pleurisy* is most often the cause. Pneumonia, as a complication of

typhoid fever or other infectious diseases, may also be a cause. In such cases we have, without doubt, to deal with hypostatic processes. In the largest number of cases, however, the history will show that the disease originated in childhood.

According to my experience in practice among children the *development of this disease* occurs in the following manner:

The infiltration which, as in catarrhal pneumonia, is to be found in both lungs, but in one more markedly than in the other, remains even after the fever ceases and an improvement of the general health sets in. For weeks, and even months, percussion reveals the same considerable dulness, the same bronchial respiratory sounds are heard, but the catarrhal râles become weaker and are more confined to the chief site of the disease. After a while bronchial respiration becomes less marked, slight inspiratory murmurs become audible in places, especially at the border of the lungs toward the unaffected parts. But, altogether, the change is not great: the dull percussion sound remains, the râles begin to grow louder. On the side opposite to that on which the disease was most violent, all the symptoms tend more and more to disappear, and the smaller spots of infiltration, which were present, are concealed by the gradually developing general emphysema of this lung. Thus the disease progresses; nearly always one lung is retracted, and, at a very late period, distinct cavernous signs appear, during which time the other lung increases in volume, and the diseased internal portion of the lung is concealed by dilatation of the surface.

In cases where the disease is fully developed the *retraction of one side* is most often established and shows the most advanced symptoms. In consequence, this form of the disease must be considered as an independent one, and requires special consideration.

All the changes found can be readily explained by the fact that one-half of the thorax has diminished in volume, and that compensatory changes have occurred in the neighboring organs.

This most clearly shows itself with regard to the thorax, and usually, also, along the spinal column.

The diseased side of the thorax is smaller in all of its dimensions than the healthy side. The ribs are closer together, so that

the intercostal spaces look smaller. The shoulder of the diseased side is lower, and the scapula is so directed as to appear wing-like. Generally, the pectoral muscles over the contracted side show wasting, thus causing the difference between the two sides of the thorax to become more apparent.

Upon directing the patient to take a deep inspiration it will become quite clear that the expansion of the diseased side is much less than that of the healthy one, and sometimes the former appears to be almost immovable. In children and youths there may occasionally be seen an inspiratory retraction of the lower margins of the ribs on the diseased side, especially when deep and rapid respirations are taken.

The spinal column is usually curved with the convexity directed toward the diseased side. Above and below will be found compensatory curves.

The body shows an inclination toward the diseased side—often to a very high degree.

The *diaphragm* and *mediastinum*, with the surrounding organs, also take part in filling up the space.

The *diaphragm* is drawn upward on the diseased side, and its position is therefore different on the two sides of the chest. The adjacent abdominal organs always follow the diaphragm—on the right side the liver, and on the left the stomach and a few loops of the intestines.

The *mediastinum* is also always carried toward the affected lung. It no longer forms a plane with two vertical surfaces, but there is a pronounced convex curvature toward the diseased side. It is followed by the enlarged and emphysematous lung of the healthy side.

The *heart* is also drawn toward the affected lung.

The diminution in the capacity of the retracted side causes, upon percussion, signs which indicate that a smaller quantity of air has been thrown into vibration, *i.e.*, diminished resonance, or that, in pathologically formed cavities, connected columns of air have been made to vibrate, thus producing a tympanitic note, with or without a metallic quality. Auscultation furnishes corresponding data.

The *physical examination* yields the following results:

Inspection, for the practised eye, is sufficient to determine, at the first glance, the location and extent of the retraction. Laennec[1] has remarked that the difference between the two sides is greater in appearance than it is shown to be by actual measurement.

The *kyrtometer* of Woillez, or a simple strip of lead, is used to represent permanently the differences in the sides of the chest. For measurement of the antero-posterior diameter the callipers must be employed, and the results will then be very accurate. The tape-measure will give the number of inches in circumference. Care must be taken to keep the tape upon one line, and this is not always easily done. But both methods are of no particular importance except, perhaps, in medico-legal cases.

In percussion it is of the greatest importance to mark out exactly the limits of the various organs. We cannot too strongly urge upon those who are not quite familiar with the subject, to clearly mark out the precise boundary lines on the skin. Otherwise they run the risk of being unable to differentiate the confused variations in resonance.

In making the drawing, I have lately made use of the patent copying-pen of E. & R. Jacobsen, which I saw employed last year in Bartel's clinic. This suits me better than the older methods.

In my examination I begin by defining the position of the diaphragm on both sides, and then the boundaries of the heart in all directions. At the same time, this usually gives an idea of the position of the mediastinum from percussion over the lung of the healthy side.

Then follows the examination as to the freedom of motion of the borders of the lungs.

Then comes percussion over the symmetrical portions of each lung to ascertain whether there is dulness or if cavities exist.

In this manner we can make a ready survey, and the results of percussion alone will give definite data.

The chief condition necessary for accurate definition of the boundaries of the organs is quite light percussion. Unless this rule is observed, the emphysematous lung of the healthy side and the marginal emphysema of the diseased side will produce

[1] L. c., Vol. II., p. 117.

great confusion. This is of greater importance when the examination is made on the left side on account of the tympanitic sounds produced by the stomach and intestines.

In comparing the percussion of the two sides, it may become necessary to use considerable force. In gentle percussion, it is possible that cavities of considerable size, which are surrounded on all sides by emphysematous pulmonary tissue, might be overlooked. It is preferable to examine first with gentle and then with more vigorous percussion.

The results of percussion must be accepted with caution, as mistakes are quite easily committed. I will point out several sources of error.

If the lower lobe of a lung is retracted, and the upper one healthy, we may be led to believe *that dulness is present in the upper lobe of the lung on the opposite or healthy side.* The reason of this is that the tissue of the upper lobe of the diseased lung is emphysematous, and, therefore, contains more air than the corresponding portion of the healthy lung. If care is taken, we obtain, as a rule, Biermer's "bandbox sound" (Schachtelton) over the upper lobe of the diseased lung. Only a very inexperienced ear would mistake this sound for tympanitic resonance.

When, by reason of the *retraction of the lower lobe of the left lung*, the diaphragm with the stomach and intestine stand in a higher position, mistakes may be committed by regarding the tympanitic sound given by these organs as the resonance of a cavity. To provide against this source of error, percussion must be performed from above downward, and great attention paid to the differences in the pitch and quality of the sounds. We shall then find, in the large majority of cases, that the sound over organs which are undoubtedly situated in the abdominal cavity, is the same as that obtained over the thorax. In these cases light percussion is specially indicated.

Another differential sign is the fact that the pitch of the tympanitic sound given by the abdominal organs does not change on opening and closing the mouth.

A distinct separation of the margin of the *infiltrated lower lobe of the right lung* from the *liver* is sometimes very difficult. But by light percussion from above downward even this differ-

ence may be made apparent, as the retracted portion of the lung is rarely absolutely free from air. This small quantity of air in the retracted lung may be sufficient as a mark of differentiation when contrasted with the absolutely solid tissue of the liver.

It may be very difficult to determine whether a tympanitic sound, whose pitch changes on opening and closing the mouth, originates in a pathological cavity or in a large bronchus surrounded by infiltrated lung-tissue.

There is greater danger of error when we examine the upper lobes of the lungs than when we examine the lower.

If there is undoubted pulmonary infiltration, a single examination by percussion may furnish doubtful results. Auscultatory signs may be of assistance, but if this is not so, the examination must be carefully repeated several times.

The contents of a cavity will change from time to time as to the relative proportion of liquid and air contained within it. This is not so with regard to the bronchial tubes. We must, therefore, pay attention to the pitch elicited at the consecutive examinations. If a change is detected, a pathological cavity is very probably present.

Under certain circumstances a change in the position of the patient will lead immediately to a diagnosis.

Gerhardt has remarked that the length of a column of air in a cavity must change when the latter has movable liquid contents. The situation of this fluid, whether it covers the most deeply situated wall in a thin layer, or whether, having accumulated in one spot, it occupies a considerable portion of the empty space, will affect the length of the vibrating column of air, and, therefore, the pitch of the sound produced by percussion. Changes in the position of the patient during the examination will cause gravitation to act in different directions, and thus modify the pitch of the sound. This would prove the existence of a cavity.

The effect of a thick pleuritic adhesion, or of infiltration of the pulmonary tissue upon the diminution of resonance, can scarcely be determined by percussion alone, as the asymmetry of the thorax, which is always present in such cases, introduces new confusing elements. The vocal fremitus is, therefore, not decisive.

With regard to the freedom of motion of the margin of the lungs, it must be remarked, that sometimes, while quite a large portion of the pleura is adherent, a narrow margin of the lung may remain free. Deep inspirations cause expansion of this portion, and it may then cover a part of the heart or liver. It follows, therefore, that slight mobility of the border of the lung does not exclude the possibility of adhesion of the pleural surfaces.

Of very great importance in the diagnosis are the changes in the positions of the various organs. In this respect mention must first be made of the heart.

The *heart*, in most cases, is drawn over toward the retracted lung. In addition, the organ follows the diaphragm, and moves upward.

These changes in the position of the heart may be very great. On the left side the *apex-beat* may sometimes reach the axillary region, and move upward by a whole intercostal space. It is stated that, on the right side, the apex-beat of the heart may be as high as the fourth intercostal space, near the sternum. Neither Nothnagel,[1] who mentions this circumstance, nor myself have ever had the opportunity to see such a case. I agree with Nothnagel in the statement that when the retraction is on the right side the apex-beat occasionally cannot be found, because it is masked by the emphysematous left lung.

Traube has stated that the position of the *pulmonary artery* is entirely changed in very marked retraction on the left side. This vessel can be recognized by the diastolic beat following the systolic impulse, and which is due to the closure of the semilunar valves.

In the normal condition the pulmonary artery begins at a point situated one or two centimetres from the left margin of the sternum. Torsion of this vessel, produced by retraction of the tissue of the left lung, can only be accepted positively when it has been drawn several centimetres to the left; that is, when it pulsates three or four centimetres to the left of the margin of the sternum.

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[1] Ueber Diagnose und Aetiologie der einseitigen Lungenschrumpfung. *Volkmann's* klin. Vorträge. Nr. 66, S. 5.

The change in the position of the pulmonary artery by the retraction of the tissue of the right lung may also be considerable. In this case it is not so easy to make out its situation with certainty; the aorta may also be felt by the palpating finger.

The closure of the valves of the displaced pulmonary artery can be appreciated, because there is diminished resistance to conduction between the vessel and the chest-walls. Infiltration of the lung, or its removal from the chest-wall (more often the latter), causes this diminution of resistance.

Traube and his school also attach importance to the increased pressure in this vessel. I think it better to speak of an increase in the difference of the pressure between systole and diastole, but I do not attach much importance to the matter.

Displacement of the mediastinum is of very great importance in making a diagnosis of retraction of the lung of one side.

It is known that the mediastinum lies on the line formed by the left margin of the sternum, and at the height of the fourth rib, on the left side, the cardiac dulness begins quite close to the sternum. If, now, the heart and mediastinum, in consequence of retraction of the left lung, are drawn to the left side, the right emphysematous lung follows, and a clear, resounding strip of lung—usually furnishing the "box" sound—presses over the left border of the sternum into the left thorax. The *cardiac* dulness, and that of the retracted lung-tissue—which it is sometimes very difficult to differentiate from one another—*begin, in this case, not, as normally, at the margin of the sternum, but sometimes five or six centimetres to the left.* By careful lineal percussion this can occasionally be determined, even when there is but slight retraction of the lung. As far as my knowledge goes, Traube[1] was the first to attach importance to this fact.

In retraction of the right lung, the change in the position of the mediastinum must be much greater, in order to enable the left lung to project into the right thoracic cavity, as the distance to be passed by the left lung—the entire width of the sternum, or, at least, two or three centimetres—is greater. In addition, two-thirds of the heart is situated to the left of the median line;

[1] Ges. Abhandlungen. Bd. 2, S. 438 ff.

all this mass would have to pass the right border of the sternum before the left lung could reach it.

As the retraction on the right side is less, this change does not take place. If it should be present, the other changes will be so extreme that it would be of very little diagnostic value.

From the complexity of these symptoms it must be apparent that the value of *auscultation*, in the forms mentioned, is extremely variable.

Still, some of the physical changes in contraction of the lung are *always present*, and their influence on the respiratory sounds is therefore constant. The principal one of these changes is the slight mobility of the affected side, in consequence of which all of the respiratory râles are less distinct.

It is to be remembered that, on account of the constant secretion of mucus, the permeability of the bronchial tubes is subject to variation, and that the most variable auscultatory signs may be presented by a patient within a very short period. Where, a few minutes before, no sound was heard, there may be pronounced bronchial respiration, or such a loud metallic sound as to be painful to the ear, and *vice versa*.

This circumstance must be borne in mind if we wish to avoid gross mistakes. Very often pneumo-thorax or pleuritis, as also phthisis florida, has been diagnosticated by an observer who has had really to deal with a cavity which is sometimes filled with fluid, and again with air.

To avoid this error, it is necessary to examine the patient several times daily, and cause him to cough vigorously before auscultating.

Pathognomonic râles do not exist in retraction of the lung. It is necessary, however, to call attention to a *rattling sound* which it is difficult to describe, but which, if once heard, cannot be well mistaken for anything else. Of medium fineness, it is to be heard usually at the height of inspiration for a short time; it spreads over larger surfaces, does not change during cough, and partakes of the characters of the pleuritic friction sound and the crepitant râles. I call it *cirrhotic crackling*, and think my attention was first called to this sign and its name by Bartels.

As to the cause of cirrhotic crackling I cannot say positively. I believe that it originates in the smaller bronchial tubes affected by catarrh and surrounded by infiltrated lung-tissue.

The cirrhotic crackling is usually heard quite uniformly over the retracted lung.

Possibly the sound termed *craquement* by Fournet is identical with that just described.

Skoda[1] does not attach much importance to it. Wintrich[2] says it is interesting from a practical point of view.

According to Fournet, the craquement is to be heard when tubercular infiltration begins to soften, and is heard with special frequency at the apices of the lungs. It is known that the retraction occurs more frequently at the apices of the lungs than in other portions.

Extensive retraction of the lung of one side is a disease easily recognized, but small, deeply-situated foci may only be revealed by the expectoration. At the most, it becomes possible to temporarily make an auscultatory observation which will be of assistance.

The same may be said of retraction of both lungs. If it is quite considerable, some difficulty will, perhaps, be experienced with regard to its pathological character, but none with regard to the diagnosis by physical exploration. It is very different when the infiltrated tissue is diffused in small patches over both lungs, as is sometimes the case after whooping-cough. In this case compensatory emphysema always surrounds such a focus, and this is the reason why the physical examination fails to elicit a satisfactory result.

These patients are really more affected with emphysema than with retraction of the lungs. The form of the expectoration when bronchial dilatation has occurred, or sometimes a violent hemorrhage, may make us suspect a more profound disturbance, the location of which can only be found at the post-mortem examination.

I do not attach great importance to it, but will mention that after *hemorrhage or fresh catarrhs* the patient complains of uneasiness in one or both sides of the chest. This does not appear

[1] L. c., S. 126–127.

[2] L. c., S. 171.

to be real pain. Pressure and tension are complained of more frequently than lancinating pains. No pleurisy can be detected. I consider it possible that small fresh retractions in the lungs may cause these sensations.

Occasionally, but not often, *the interstitial pneumonia may progress, in which event extensive infiltration may occur in place of the emphysema.*

With more or less elevation of temperature—I never found elevation of temperature in old people, even when testing for it twice a day—and constant cough, this change sets in after a number of months. In the few cases of this kind observed by me during the last few years in Tübingen, the disturbance of the circulation was greater than that of respiration. My observations only referred to old people. The physical examination showed the development of the disease.

It is so easy to confound this affection with slowly developing true tuberculosis in emphysematous lungs, that it is very difficult to differentiate them from one another.

An interesting circumstance is to be mentioned. In cirrhosis after catarrhal pneumonia the primary infiltrated foci may be concealed by emphysema in the vicinity; but in this disease the reverse obtains. The emphysema gives place to interstitial pneumonia.

The last described conditions constitute, in a certain sense, *transitions to the forms of interstitial pneumonia which are allied to phthisis.*

In this case the differential diagnosis is more difficult, as positive symptoms showing the dissimilarity are not present, and nothing but the manner of the development of the disease in certain special cases will enable us to arrive at a conclusion.

The general condition and activity of the patient are to be considered as of first importance in distinguishing it from phthisis. The local signs are of less value.

Infiltration of the pulmonary tissue, especially when situated in the upper lobes, signs of cavities, constant expectoration of muco-purulent matter, are symptoms belonging as well to the forms of interstitial pneumonia allied to phthisis as to the diseases that have been described.

Very often the disease is located in the apices of both lungs, or in the apex of one lung and the lower lobe of the other. The development of the disease may occur in such a manner that interstitial pneumonia follows pleurisy or pneumonia in the lower lobe of one lung, while the upper lobe of the opposite lung is already the seat of the same disease. Or interstitial pneumonia, induced apparently by a chronic catarrh, may attack the upper lobe of a lung after the same process has caused retraction in the lower lobe.

I do not believe that I am mistaken in the opinion that more or less extensive retraction makes the healthy portion of the lung so affected more liable to become the seat of interstitial pneumonia. This will be easy to understand if my explanation of the origin of the interstitial pneumonia should prove correct.

This spread of the disease to healthy portions of the lung is attended by febrile movement. Under these circumstances a longer or shorter period must elapse, during which it will be impossible to say whether phthisis exists or not.

If this is is not the case—if phthisis is not present—there will come a time when the symptoms remain stationary, and I refer to this in making the following statement.

I do not hesitate to diagnosticate interstitial pneumonia and exclude phthisis, so long as two conditions are present, viz., great physical and mental activity, and a steady and vigorous impulse of the heart. Apparently these two conditions are incompatible with each other, but their relation is entirely borne out by the facts.

I will here state the details of a case which came under my own observation.

In the year 1868 I first saw a patient with the following previous history:

During the first year of life the patient had a pulmonary affection which kept him confined to his bed until he was ten years of age. At this time the disease improved, and he was sent into the country. In his twelfth year he was not so well, and in his thirteenth year he had a violent attack of pneumonia, after which he was again sent to the country. In his sixteenth year he was so ill that, for a time, death was momentarily looked for. Constantly, until twenty years of age, he was a great sufferer. The use of Lippspringe water was ordered, under which he improved. The state of the patient was such that he could not attend to systematic study. Nevertheless, during the time of improvement so much ability was shown, and he made such rapid progress in his studies, that he entered the

university at the age of twenty-two years. At twenty-five years of age he was advanced, after which he followed very active scientific study. At twenty-eight he was a lecturer, and when thirty years of age was appointed professor.

I saw this gentleman for the first time in 1868, when he was thirty-three years of age, and I attended him continually from that date during the next five years.

The physical examination showed such extensive infiltration of both lungs as to make it difficult to find a spot in which bronchial breathing could not be heard. The upper lobes of both lungs presented signs of large cavities. There was no change in the position of the lungs. Heart normal.

There was constant expectoration of muco purulent masses. *Vital capacity* (average of three examinations), 2,200 c.c.

Great retraction of both sides of the thorax.—Nutrition fair; *weight of the body*, 51.25 kilo.; *height*, 172 c.c.

During this year and the beginning of the following he had blood expectoration in June, September, December, and January.

March, 1869.—The physical examination gives the same results as before. *Bodily weight*, 51.5 kilo.; *vital capacity* the same. Made a trip to Italy. Had malaria in Rome. Returned in July. Great debility with disinclination to work. *Bodily weight*, 49.0 kilo.; *vital capacity*, 2,250 c.c. At my suggestion he took a trip to Switzerland, and exercised moderately in mountain walking (ascending mountains 8,000 feet high). Returned in September, apparently well. Weight of body had increased to 53 kilo., vital capacity to 2,300 c.c.

During the following year he was again working very hard; had several hemorrhages of the lungs, one (1871) being so severe that he was completely prostrated. He recovered in a short time, but often complained of sleeplessness caused by the great irritability of the nervous system.

The patient's condition remained very much the same during the remainder of the time he was under my observation, excepting that his general health improved, and with this improvement his extraordinary capacity for work increased. Death took place in 1874, and was due to an acute croupous pneumonia of both lungs, combined with pericarditis lasting six days. The post-mortem examination showed "cavities in the apices of both lungs, and firm, old adhesions between the infiltrated lungs and the pleuræ. Heart flaccid, but of normal volume; the valves intact." I am indebted to the kindness of a colleague for these last data.

In this case it is evident we did not have to deal with phthisis. In more than five years the bodily weight remained the same, the severe changes in the lungs did not progress; the bodily strength was sufficient to enable him to ascend mountains 8,000 feet high, and it would evidently be absurd to say that phthisis existed in this case. But, apart from this, we should remember that there was, during the whole time, not only sufficient but unusually good cardiac action. The patient's pulse remained

between 60 and 70, was full and strong, and even after severe hemorrhages did not show much increase in rapidity. Exercise did not accelerate the heart's action immoderately. I never observed any fever in the case, and even in the beginning of the fatal croupous pneumonia the temperature remained at the comparatively low point of 39° C., only rising on the fourth day to 40° C.

I have mentioned only one, and that the most marked case of the many observed by me. All of these cases were characterized by the peculiarities mentioned above, viz., great capacity for work, and strong heart's action. Too much importance must not be attached to the general nutrition, as a symptom. The original normal condition is the proper point for comparison, as daily observation teaches that many persons remain lean despite the fact that the ingested food is enormous in amount, while others grow fat upon meagre fare. I willingly acknowledge, however, that the rotundity of the body usually disappears in such severe pulmonary changes, but this rule has so many exceptions that we cannot rely implicitly upon it.

Nor would I attach too much importance to the *temporary appearance of febrile movement.* A broad distinction must be made between elevation of temperature lasting for weeks, and that occurring only for a short period. The former is always a grave condition. Although it does not prove absolutely that phthisis exists,—I have seen a stationary condition, which continued several years, develop after fever had lasted for months,—it is, nevertheless, a symptom of the local progress of the pathological process which must shorten life. Prolonged fever is always injurious to the general condition of the patient, and the more so when the system is already considerably debilitated.

I only attach importance to *hemorrhages* when they are profuse in quantity. *They are more frequent in the various forms of interstitial pneumonia than in true phthisis.*

All forms of interstitial pneumonia may terminate fatally in true tubercular phthisis. When such a complication sets in the clinical history of the disease changes at once. This is illustrated by the following personal observation.

Mrs. B., twenty-six years of age, came under treatment in the Policlinic, February 19, 1875. When eight years old she had measles, which kept her down for several months. Aside from this she had never had any disturbance of respiration; no cough; perfectly able to work. She had married young, and was the mother of three children.

During the past winter she had suffered from a frequent harassing cough, pains in the chest, and dyspnœa on making any considerable physical exertion.

Examination showed decided shrinking of the left lung; the heart displaced toward the left; the diaphragm elevated on that side; curvature of the spine with retraction of the left side; compensatory overdistention of the right lung, which crowds considerably over the border of the sternum toward the left. In addition to all this, there is recent bronchial catarrh with moderate fever (101° F. at evening). *Diagnosis:* Cirrhosis of the left lung with recent catarrh.

In the course of a few days the patient grew worse. There was high continuous fever, extensive catarrh involving also the finer bronchi, and great loss of strength. *Diagnosis:* Acute miliary tuberculosis, principally localized in the lungs.

Without any specially prominent symptoms *death ensued* on the 22d of March.

Autopsy (Schueppel).—The anterior border of the *right lung*, which on opening the chest hardly collapsed at all, extended toward the left about two centimetres beyond the left border of the sternum. The *pericardium* was correspondingly drawn toward the left, and a large portion of it lay in contact with the walls of the thorax. The *left lung* had so far receded upward and backward that the anterior border of the upper lobe corresponded to the line of union of the ribs with the costal cartilages.

The *right lung* was large and almost entirely free, with but loose attachments to its surroundings at some few points. The pleural coat was slightly reddened in spots, and disseminated with numerous, mostly very fine, grayish white miliary tubercles. The upper and middle lobes were emphysematous; in the neighborhood of the apex there was a small, cicatricial depression, and beneath it a cavity fully the size of a pea, smooth-walled, and containing pus. The upper lobe was, in the main, pervious to air, and contained but a scanty blood-supply, although it was thickly and almost uniformly disseminated with innumerable groups of grayish white miliary tubercles. It likewise contained several calcareous deposits, the largest of which were of the size of a cherry, studded with fresh tubercles about their periphery, and containing a small caseous nucleus at their centre. The middle and lower lobes contained traces only of older, slate-colored, deposits, though these portions also were thickly sown, throughout their entire extent, with uniformly distributed, very closely aggregated, gray miliary tubercles. The *smaller bronchi* contained gray, turbid mucus—their mucous membrane showing nothing abnormal. The *bronchial glands* were relaxed, soft and juicy, showing spotted pigmentation—to the unaided eye they seemed free from tubercles.

The *left lung* was pretty well grown fast at its base, its posterior surface and

its apex being firmly united with the costal pleura. The lung was smaller, being especially diminished in depth. The tongue-shaped portion of the upper lobe was greatly shrunken. At the posterior portion of the lobe, an inch below the apex, there was a cavity of the size of a walnut, with tolerably smooth walls, filled with a gray, unctuous mass. The anterior border and the tongue-shaped projection of the upper lobe were devoid of air, firm, of a slate color, partly the seat of caseous infiltration and partly studded with fresh tubercles in process of degeneration. The *bronchi* were dilated and filled with pus.

The lower lobe felt harder, but, although containing air, was very thickly studded with tubercles of a grayish white quality, which were so closely crowded together as to be almost confluent. At the apex of the lower lobe there was a cavity of the size of a bean, filled with pus. The bronchial tubes were like those of the left side above;—the same was true of the bronchial glands.

With regard to the conditions found in *other portions of the body*, we need only mention the presence of tubercles in the liver, the spleen, the kidneys, and on the peritoneum. The abdominal extremity of the left Fallopian tube was greatly swollen and thickened, its walls the seat of a diffuse caseous infiltration, extending almost to the uterus, and the tube filled with pus. The lower portion of the ileum contained a number of cheesy follicles and little lenticular ulcers.

We here have an instance in which a catarrhal pneumonia, following measles during the eighth year of life, led to retraction of the lung. In spite of the possibility of auto-infection from caseous masses, general tuberculosis did not arise until after so long a time. The slight tubercular outbreaks of an earlier period, the existence of which seemed to be indicated by the autopsy, do not appear to have materially disturbed the general health. In the last general eruption of tubercles, the picture of the disease was present from the very beginning.

The *third* group still remains to be noticed, viz.: *bronchiectasis, with evidences of putrescence in the expectoration.* It presents a picture which even Laennec placed by itself, recognizing it as peculiar.

In my delineation thereof I follow Biermer.

The principal feature of the affection lies in the *character of the expectoration.*

This, although varying in amount, is, as a rule, quite abundant, as much as 600 c.c. being evacuated in a day. Trojanowsky even states that he has himself observed as much as 800 grm. during a day. It would be a mistake to expect always to

find very abundant expectoration in the victim of bronchiectasis. This, of course, is the case if one or more cavities of the size of a fist exist in the lungs. At other times, however, the expectoration for a long time remains moderate, until a catarrh, spreading over a larger area of mucous membrane, excites more abundant secretion.

The manner in which patients cough is furthermore characteristic. The principal amount of sputa is evacuated not by means of many acts of coughing, repeated at short intervals and quite uniformly distributed through the day, but by a few paroxysms rapidly following each other, and succeeded by some hours of rest. Where there is a very abundant accumulation, the act of raising it is, as a rule, accomplished with no special effort; the whole mouth is filled and emptied at once. Such a paroxysm often comes on in the morning on waking, probably when the patient has lain in such a position that the affected side has been most dependent, and alters this position on rising.

This peculiarity of the cough and the raising is referred to two circumstances. The bronchial tubes, so far as they are dilated, become less irritable, and even tolerate the irritation of a highly decomposed secretion without being immediately aroused to a reflex cough. This does not take place until the decomposing mass comes in contact with a comparatively normal portion of mucous membrane. The dilated bronchi constitute a reservoir in which the mucus secreted by their walls may accumulate. This reservoir is not emptied until it is full enough, so to speak, to overflow, a condition which, when quite full, may be brought about by a slight change of posture. In addition to this, the comparatively healthy bronchial mucous membrane in the neighborhood becomes, in a certain sense, accustomed to its constant exposure to one and the same irritant.

The *matter expectorated* is always more or less rich in pus, and uniformly contains mucus. Aside from its solid ingredients, it usually contains a large amount of fluid. *If the secretion from a larger bronchiectatic cavity is therefore allowed to stand in a suitable vessel, it will divide into three layers.* The lowest will contain the corporate constituents, presenting greenish, yellow, or yellowish gray, or even whitish gray homogeneous masses, seldom rolled up in nummular form, generally surrounded by floating threads of mucus. Then follows a layer of turbid, greenish yellow fluid, holding but little suspended in it, and con-

stituting the largest of the three portions. On the surface there is a layer of muco-pus, which is mingled with air-bubbles, and thus kept afloat.

Even at the very time of their expectoration the sputa have a very foul odor, sometimes amounting to an intolerable stench. It is by no means uncommon for these patients so to pollute their surroundings as to make them very repugnant to others, and to render immediate contact with them unendurable. Then the fetor of the bronchial secretion also communicates itself to the breath.

Microscopical and chemical examination of this expectoration has revealed the following:

The sediment at the bottom, in addition to the presence of more or less disintegrated pus-corpuscles, presents peculiar yellowish white plugs, varying in size from that of a millet-seed to that of a bean. These were observed as long ago as by Dittrich,[1] and were more accurately described by Traube,[2] and finally by Leyden[3] and Jaffe. These plugs contain at first pus-corpuscles, with detritus, then fat appears in them in the form of drops; at the same time they change their color from white to a dirty gray. Finally, they present crystals of the fatty acids—so-called margarine crystals—those from the fresher plugs appearing as smaller, shorter, and finer needles, those from the older ones as thicker needles or bundles of needles, which are slightly bent and display varicosities under the pressure of the covering glass.

This description of Traube's was supplemented by Leyden and Jaffe with the statement that the apparently amorphous detritus consists of fine granules and rods, which belong to a fungus growth. These gentlemen are of the opinion that the fungi of the lungs are descendants of the leptothrix buccalis, which is regularly to be found on the mucous membrane of the mouth. They regard the alteration in form of those specimens found in the lungs as due to their altered place of abode. Aside from these, other and changeable forms arise, to which, by reason of this very changeableness, no special significance is to be attached.

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[1] Ueber Lungenbrand in Folge von Bronchialerweiterung. Erlangen, 1850.

[2] Gesammelte Abhandlungen, II., pp. 556 and 684 et seq.

[3] D. Archiv f. kl. Med. Bd. II., 1867, p. 488 et seq.

Traube denies the occurrence of elastic fibres in the sputa; to which I would reply, with Biermer, that in rarer instances they are certainly to be found. An unpractised observer must be on his guard to avoid confounding them with needles of margarine.

In making a *chemical analysis* of these expectorated substances we encounter a twofold series of products of transformation—those which arise from the putrefaction of albuminoid substances, and those which arise from the decomposition of neutral fats. Sulphuretted hydrogen, ammonia, leucin, and perhaps tyrosin, belong to the putrefaction of albuminoids, and their presence has been demonstrated by Bamberger, Leyden, and Jaffe. Crystalline, fatty acids exist in large quantities, but the lower members of this class are also regularly to be found, viz., formic, acetic, and butyric acids (Bamberger). Glycerine only showed itself in traces, according to Leyden and Jaffe, and not regularly even in such small quantites.

It is further to be observed that, on the addition of a dilute iodine solution to these plugs, a brownish yellow, violet blue to purple violet coloring arises, especially on the fungous growths and the investing layer lying next to them (Virchow, Leyden and Jaffe). Leyden and Jaffe have shown that any muco-purulent sputum, standing exposed to the air, undergoes changes quite similar to those of a specimen originating in a bronchiectatic cavity, and having undergone putrefaction there. It is true that it required weeks before the higher grade of decomposition was attained, viz., the development of crystals of the fatty acids. This difference in the time required may, perhaps, be explained by the higher temperature of the living body. There can, therefore, be no doubt that a process of putrefaction has taken place within the air-passages when sputa such as those described are evacuated. On the other hand, the influence of the leptothrix masses in bringing about this state of putrefaction is by no means established.

Leyden and Jaffe did, indeed, find formed bodies in the sputa decomposed in the air similar to those demonstrated in the sputa of persons with putrid pulmonary disease, but they do not venture to decide whether they are identical.

One point worthy of note is the failure of the iodine reaction in the exposed sputa, while it occurs with great regularity in that expectorated from the lung.

The question which always arises in connection with fungous diseases here obtrudes itself upon us again: Do the fungi, which are undoubtedly present, primarily cause the pathological disturbances, or does some other exciter of disease induce changes which, besides causing other deviations from the normal, create the possibility for the development in masses of the fungous germs which are everywhere present. Not all writers, unfortunately, are as guarded in their expression of opinion as Leyden and Jaffe.

The processes of putrefaction always require a certain amount of time for their accomplishment. The question of how long this requires when the external conditions—moisture, warmth, the free access of air—are as favorable as within the air-passages, has not yet been sufficiently investigated.

It is true that we have been in the habit of casting all the blame upon the two conditions of stagnation and retention of the secretions. But when we see the quantities evacuated once or twice a day from large, sack-shaped bronchiectatic dilatations, and remember that these have only required a few hours to undergo advanced changes, we cannot suppress the wish that investigation by means of experiments might throw some more light upon the conditions of putrefaction under these circumstances.

This wish can only be still further intensified by the observation of those rare instances of primary putrid bronchitis, in previously quite healthy lungs, among people who live under the most favorable external conditions. Our experiences thus far are, in fact, not sufficient to give us a clear understanding of these things.

Physical examination can sometimes furnish us with the assured demonstration of a cavity. But we must remember that even large cavities are not to be found if they lie further from the walls of the chest, and are surrounded with emphysematous lung-tissue, or if they are filled with fluid contents.

In the latter instance they may be found by an examination undertaken soon after the evacuation of their contents, which, in the majority of cases, takes place in the morning. With regard to the former class I would refer my reader to the remarks made above, to which I have but little to add.

Earlier writers (Rapp, Biermer) have shown that vesicular breathing is sometimes to be heard over bronchiectatic cavities. Obstruction of the bronchus leading thereto, or the filling of the cavity itself, permits the auscultatory sounds of the surrounding parts to be heard.

If pervious lung-tissue lies in contact with the walls of the chest, and a cavity is situated in the depths behind it, the auscultatory signs of the two regions will, as a rule, be most clearly distinguished if auscultation is practised first with the stethoscope and then with the unaided ear. It is important that the funnel of the stethoscope should not be too large. Then the sounds produced within the area covered by the stethoscope are obtained pretty well isolated. Listening then with the ear alone we obtain the impressions of sound from a much larger area.

By causing the patient to breathe more deeply or more superficially, we gain further assistance in distinguishing between the more superficial and the deeper portions.

Auscultation by means of the stethoscope affords less perfect conditions of conduction than the direct application of the ear to the chest. As the sound-waves are derived from a smaller area their sum is less. Those sounds proceeding from the depth have greater obstacles to overcome than those developed nearer the surface, especially here where the sound must pass through normal lung-tissue, with its successive layers of unequally dense media—air, and solid tissues.

Now, if we cause the patient to breathe superficially we shall hear exclusively the vesicular murmur produced in the area immediately under the instrument—it may be weak, but it will still be distinct. Immediate auscultation, with deep inspiration on the part of the patient, will give us a different result. A larger number of sound-waves reaches the ear, better conducted and from a larger area, some of which belong to the deeper and some to the more superficial portions of lung. The practised ear distinguishes the one from the other without difficulty, because it has had the opportunity of comparing them with those originating in the superficial portion alone.

It is just like listening to an orchestral performance. From a greater distance a musician may indeed recognize the melody but not be able to distinguish the sound of the individual instruments. This is only possible on approaching within a certain distance of the point of origin of the tones. But he who stands close to the base-drum or kettle-drums is liable to lose the sound of the violin. By a judicious choice of distance it is possible, however, to hear just what one wants to hear.

By the same method, sounds, which would otherwise be drowned, may be recognized in the presence of loud râles.

Biermer justly remarks that the râles of bronchiectatic lungs are marked by their moist and coarse quality, which is not sur-

prising since they originate in wide cavities and amidst thin fluids.

Percussion rather falls into the background as a method of investigation in these conditions, inasmuch as cavities surrounded by normal or emphysematous lung-tissue can very often not be demonstrated by this means—as was shown even by Stokes.

It is furthermore important to remember this fact, that *in bronchiectasis more frequent changes take place in the signs furnished by physical examination than in any other pulmonary disease.*

Among the manifestations which may arise in pulmonary cirrhosis with bronchiectasis in all its forms, there are a few which are worthy of special mention.

Fever occurs in connection with the *development* of this process; when it is associated with the *completed* process it always points to some complication.

Although it is not possible for us clearly to understand what influence an interstitial pneumonia, as such, has upon the temperature of the body, we may lay it down as an established fact that an elevation of temperature is associated with the *development* of this malady. This is a fact of experience, which we accept without asking what share in the production of the fever is to be attributed to a coexisting catarrh, a pneumonia in process of gradual resolution, and the like.

It cannot be claimed that there is any special tendency to febrile disturbance in fully developed and completed interstitial pneumonia. Quite the contrary. It would rather appear as though such persons were hard to throw into a fever, and that when it does occur the body temperature remains rather low. There are exceptions to this, however, and a simple fresh catarrh may lead to an elevation of temperature, as in a well person.

The statement can hardly be doubted that *putrefaction of the retained bronchial contents does not at once, and as a matter of course, give rise to fever.* In proof it is quite sufficient to point out how often a large amount of putrescent material is expectorated day by day for years, without the thermometer rising even so much as a few tenths of a degree. In view of this fact it seems rather an assumption to refer occasional paroxysms of

fever to the absorption of putrescent masses which one imagines are imprisoned. We then conclude from the fever that absorption has taken place, and from the fact that fever has been produced, that putrescent changes have occurred in secretions retained in the bronchial tubes by reason of some obstacle to their evacuation. The only point which is proven, is that the absorption of putrescent substances into the blood may give rise to elevations of temperature.

The only support that can be adduced in favor of the popular opinion, is that furnished by the few but interesting experiments of Gerhardt.[1] In bronchiectatic patients who were feverish, he found, in two cases, that whenever systematic compression of the thorax was exercised, whereby a more copious evacuation of decomposed mucus was effected, the body temperature was lowered. These observations are, however, as yet too few to serve as the basis of general conclusions. At the same time they also admit of explanation on my theory.

It appears to me that a different explanation is at least equally justifiable.

The bronchial mucous membrane of those portions of the lung which are the seat of the decomposing masses, is so thickened as to admit of but slow passage of anything into the blood-current; hence, such small portions of the decomposed, fever-exciting material ever arrive in the blood at one time, that they are capable of being overpowered in the metamorphosis of tissue. It is also possible that under constant exposure to its influence the body may acquire a certain tolerance of this as of any other poison. This would explain why, despite the most extreme foulness of the secretion, bronchiectatic patients are not always feverish.

But if by any means some of the putrescent mass comes in contact with other hitherto free portions of mucous membrane—a fresh catarrh with severe cough may give the occasion for this—then the possibility of absorption is incomparably greater. Furthermore, the secretion thus transplanted produces a local inflammation, not only with increased secretion, but also with new putrefaction in this mucus. My theory is materially supported by the post-mortem conditions of those bronchiectatic patients

[1] D. Archiv f. klin. Med., Vol. XV., 1875, p. 1 et seq.

who have died with the evidence of a putrid bronchitis. It is well-known that in such bodies, as a rule, there are small pneumonic deposits scattered through the lungs, originating in intruded masses of putrescence. Or, we may find in healthy lung-tissue a bronchial catarrh which is produced by the inhalation of plugs of pus.[1] Why should not the same conditions which have been abundantly proved as existing in fatal cases also exist when, by reason of the lesser extension of the process or the greater powers of resistance of the patient, life is not destroyed?

With regard to the *type* of the fever, we can only say that no definite form occurs regularly. On the contrary, there are innumerable varieties. Hectic fever is encountered as often as a more uniform elevation above the normal, in which 104° F. is seldom reached.

For this reason it is also only exceptionally possible to accept the course of the fever as a safe guide to the diagnosis of a given complication.

Night-sweats are, as a rule, not present in this disease; their occurrence would, at least, throw some doubt on the diagnosis.

Hemorrhage from the lungs is deserving of special notice.

There is so much variance in the different views held on the origin of pulmonary hemorrhages and their relation to tuberculosis, that no physician will succeed in doing more than arriving at his own conclusions from his own experience. I shall therefore attempt no exposition of the views of others, but merely remark that having practised in one place which was very rich in tuberculosis (Kiel), and in another poor in tuberculosis (Tübingen), I have found no occasion in the latter place to alter the views acquired in the former. My opinion is that spitting of blood, especially the oft-repeated variety, is far more common in the chronic forms of lung disease not leading to phthisis—the anatomical basis of which forms is interstitial pneumonia—than it is in phthisis, whether the latter be accompanied by the development of tubercles or not.

I very much doubt whether the blood effused in the air-pas-

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[1] See *Traube*, Ges. Abhandlg., II, p. 567.

sages can of itself give occasion for the development of phthisis, as was taught by Niemeyer. In some exceptional cases such a connection may exist; as a rule, it certainly does not.

I may here refer to the case narrated in detail above. Despite repeated and sometimes alarming hemorrhages from a severely diseased lung, the bodily weight, the vital capacity, and the powers of endurance generally remained undisturbed during a period of five years. It would be possible for me to bring forward not a few histories of patients of the same sort.

The pulmonary hemorrhages in interstitial pneumonia often occur at long intervals of time.

Thus, in a case coming under my observation which belonged to the emphysematous-bronchiectatic form, a woman, fifty-four years old, had suffered from severe hemorrhages in the thirteenth, forty-first, forty-ninth, and fifty-second years of her life. In other cases these hemorrhages recur more frequently and almost regularly, as in the case so often referred to.

I have often observed that *more severe hemorrhages are preceded for a few days by slight ones.* Without any special occasion, small quantities of fresh blood mingle with the usual expectoration. If the patient is observant and cautious, we may then succeed by complete mental and physical rest in preventing the heavier loss of blood. I therefore lay stress upon these *warning hemorrhages.*

We are very often in a position to discover the *exciting cause* of the hemorrhage. Then it generally appears that something has happened which is calculated to raise the arterial blood-pressure, such as the lifting of a heavy weight (I once saw a very exhausting hemorrhage immediately after the effort), forced marches, injudicious mountain climbing, disturbances of temper, rapidly developed fever, great and sudden diminution of atmospheric pressure. At other times we fail to discover a cause.

As might be supposed, the amount of blood discharged varies within the widest limits. The bleeding is liable to recur.

Some previous writers have called attention to the fact that *a fluid of the color of the serum that exudes from meat, and containing blood, may be evacuated from bronchiectatic cavities*

(Gombault, Biermer). I have seen this more frequently, but have, as a rule, found the fluid intimately mixed with fresh, glutinous mucus which contained a disproportionately small number of pus-corpuscles. The mass looked like frog-spawn slightly colored with blood, and was evacuated by my patients nearly every day. It was in the shape of rather firm lumps, sharply separated from the rest of the expectoration, and did not seem to me to stand in any close connection to the actual hemorrhages.

The origin of the hemorrhage is doubtless manifold. Experience at the bedside seems to indicate that the blood not rarely originates from the capillary system; the little hemorrhages, amounting to but a few grammes, are most easily explained in that way.

Ectasia or dilatation of arteries has been anatomically demonstrated, and may be regarded as the source of the more copious losses of blood, since such dilatations may very readily be developed under the circumstances here existing in a cirrhosed lung and in the walls of a cavity which has arisen by bronchial dilatation.

The cessation of hemorrhage occurs more readily under these circumstances than in case of ulcerative phthisical processes, through pressure upon the wounded vessels by the blood effused and coagulated within the dilated bronchi. I have repeatedly observed that a few days after the first arrested hemorrhage a fresh hemorrhage has immediately followed the expulsion of a cylindrical clot. Indeed, careful examination of the sputa of these patients, after a hemorrhage, as a rule, reveals the presence of plugs, which are doubtless casts of bronchial tubes. These are sometimes retained so long that they decompose and acquire an odor extremely offensive to the patient himself. This does not, however, seem to exercise the slightest influence on the patient's general condition, particularly not on the fever.

Hemorrhages which originate in ulcerating bronchiectatic cavities have, of course, a different significance—not in themselves, but on account of their origin.

Diagnosis and Prognosis.

According to my opinion many more diseases of the lungs belong to the group of interstitial pneumonia than are usually accredited thereto. Thus I would class the affection which Ruehle designates as chronic pneumonia of the upper lobe, not under the head of consumption, but under this head. I believe I am justified in this, both on theoretical and on practical grounds.

Consumption is a name that should surely be applied to a disease that causes rapid wasting of the body and not to one which accompanies a man from the cradle to old age, making him, it is true, capable of less labor or endurance than he would otherwise be, but by no means constituting a continued state of ill-health. Therefore this expression should be applied to those forms of disease which, in accordance with the meaning of the word, actually induce consumption, waste, or destruction.

The anatomical basis of "simple chronic pneumonia" is the proliferation of the interstitial connective tissue in the framework of the lung, with its termination in cirrhosis and the development of bronchiectatic cavities. Why should the circumstance that those forms of consumption which lead to rapid breaking down, as a rule, though not invariably, begin in the upper lobe, be considered as having such weight as to induce a severance of those processes which clinically and anatomically belong together? No one would hesitate to rank that process which is known as chronic pneumonia in the group of pulmonary cirrhosis the moment it took place in the lower lobe of the lung. What grounds exist for ranking it with phthisis because it is situated in the upper lobe? The description of the condition itself in Ruehle's article is admirable, but I must be allowed to remark that just in consequence of this description I challenge this author's right to classify his "simple chronic pneumonia" under the head of consumption.

I find a practical argument in the fact that it will be far easier for the physician at the bedside to obtain a clear insight into the process that is taking place as soon as he draws the dividing line

as I propose. And, furthermore, that many a physician and many a patient will proceed quite differently—the one prescribing earnest measures and the other carrying them out—as long as the fatal word "consumption" has not been uttered.

If one reasons from the standpoint above indicated, then the differential diagnosis between interstitial pneumonia and phthisis loses many of its difficulties.

Two questions must be kept distinct.

1. At the time of making the examination, have we consumption before us or interstitial pneumonia with one of its sequels?

2. If the latter is the case, how great is the probability that the individual in question will become consumptive?

The decision of the first question will depend greatly, as I have previously set forth, upon the strength of the patient and the behavior of his heart.

With reference to the second and more difficult question, several circumstances must be considered.

Heredity.—If the individual comes from a consumptive family, then the probability that what commenced as an interstitial pneumonia will finally lead to consumption is far greater than if the reverse were true.

Age.—The more advanced the age, the less likelihood that phthisis will be added to interstitial pneumonia.

Exciting Causes.—External injuries or wounds, hypostatic conditions, croupous pneumonia, long-continued pleurisy with effusion, are more favorable than chronic bronchial catarrh.

Chronic bronchial catarrh, caused and maintained by dust-inhalation, is more favorable than that which seems to arise spontaneously or from a slight cold.

A catarrhal pneumonia which runs its course rapidly is, as a rule, more favorable than one which progresses slowly.

Seat.—Interstitial pneumonia, situated in the lower lobe of the lung, is less likely to be associated with phthisis than when situated in the upper lobe.

Accompanying and Resulting Conditions.—The more extensive the development of emphysema, and the more sufficient the compensatory work of the right heart, the less the probability of phthisis.

Tendency to Bronchial Catarrh.—The less marked this is, the less likely will the patient be to develop consumption.

As a matter of course, the aggregate of *individual, internal, and external conditions* is of the highest significance, sometimes determining the fate of a given case. General powers of resistance—a good constitution, as we call it—a strong digestive apparatus, well-developed respiratory muscles, a skin capable of quickly accommodating itself to outside conditions—all these must be taken into account as well as the working power of the heart and the possibility of the patient's taking care of himself, and, in a few instances, being able to live entirely for the benefit of his health.

It may sometimes become a sufficiently difficult matter to determine *the point of time when the supervention of phthisis is threatened.* Under some circumstances, in highly cirrhosed and bronchiectatic lungs, physical examination fails us. In addition to the main landmark, the slow, strong pulse, I here lay stress on the *vital capacity*, but only on condition that the patient is practised in the use of the spirometer, and that we have his previous record, in this particular, as a basis of comparison. *Even if all other signs seem to argue in favor of phthisis, we need not fear any immediate danger so long as the vital capacity has not diminished and the pulse remains quiet.* I am far from undervaluing the scales and the thermometer; they, too, are accurate aids, but they rank below the other two. Accidental causes for a loss of weight or rise of fever are more frequent than the evidence of their being accidental.

The *differential diagnosis* between pure emphysema and that accompanied by cirrhotic processes has already been given above. I do not believe that the *prognosis* of these forms differs, in the majority of cases, from that of simple emphysema. If larger surfaces of lung have undergone cicatricial degeneration, or if there is extensive bronchiectasis, then the thing is different. We must add to the account the probability of an earlier failure of the heart, the possibility of a putrid bronchitis.

It is by no means always possible to distinguish a bronchiectasis, which furnishes a copious and constantly fetid expectoration, from empyema of long standing which has opened into the

bronchi. Retraction of the thoracic walls occurs in the one case as in the other; all other manifestations may present a deceptive similarity. It is only by the aid of a clear history of the case that a reliable conclusion can be reached.

I have never witnessed the *perforation outward of the pus from a bronchiectatic cavity.*

Biermer,[1] however, adduces a case which came under his own observation, and cites another from Bamberger. It will require accurate knowledge of the previous condition of the patient, whether this be obtained through our own observation or from a careful report, to guard us against confounding this condition with an empyema necessitatis, the signs of which are otherwise fully developed before us.

Putrescence of the expectoration may vary in significance both as regards prognosis and diagnosis. It may be habitual, and, to a certain extent, the contents of bronchiectatic cavities communicating with difficulty with the larger air-passages, are always decomposed without there being any special significance to be attached thereto.

A very different degree of importance is to be attached to this condition when, arising occasionally, it betrays itself both by its reaction upon the general condition and upon the local pulmonary disease.

The *danger* of these conditions, comprised under the common name of *putrid bronchitis*, is to be seen by statistics. Trojanowsky found putrid bronchitis to be the cause of death in more than one-third of the cases of bronchiectasis collected by him.

Another point of prognostic significance here is the demonstration of more or less extensive foci of catarrhal pneumonia diffusely disseminated over the lungs, but found more extensively and more frequently in the lower than the upper lobes. According to Trojanowsky, the lungs were found involved in nearly four-fifths of the cases of putrid bronchitis. The more extended the pneumonic centres the greater the danger to life. But this danger threatens even in smaller consolidations, inasmuch as the gangrene of the lung, which supervenes with com-

[1] Virchow's Handbuch, l. c., p. 744.

parative rapidity, leads *locally* to hemorrhages, to perforation and pyopneumothorax, while *generally* it increases and hastens the putrid infection. *The fever does not always afford a safe index to the degree of danger.* Often enough, normal or subnormal measurements appear toward the fatal termination. During the progress of the disease also we may sometimes find a but slightly elevated temperature.

The *pulse* may be of great prognostic value in putrid infection. A high rate of frequency, 150 and over, points with great certainty to a near end.

In addition to the point already indicated, of whether an empyema has perforated inward, the differential diagnosis may still involve the question of whether or not dilatations of the bronchi are present in addition to putrid bronchitis. Aside from the history of the case, the most important question here will be, whether or not physical exploration can demonstrate the presence of such cavities.

The *prognosis of the individual forms* is found to be most favorable in the emphysematous-bronchitic conditions in which there are smaller bronchiectatic cavities having free connection with the air-passages. Next are those forms which are mixed, representing emphysema together with consolidations of the lungs, having cavities with the free escape of their contents, consequently those, in particular, which sometimes present an entirely odorless expectoration. Those cases showing extensive consolidations, and those of ectasia with uniformly fetid expectoration, are probably equally dangerous.

Treatment.

In interstitial pneumonia we can only speak of a cure—that is, the entire cessation of all diseased processes—so far as it refers to the prevention of the results of the local disturbance. This local disturbance itself can never disappear, for the development of cicatricial tissue—which always implies a loss of pulmonary tissue—must of necessity follow the inflammation of the connective-tissue framework of the lung.

We are, therefore, obliged, from the outset, to limit our

therapeutic efforts to the task of enabling our patient to get along with the remnant of lung left him, and preventing any further loss.

These ends may be attained—

1st. *By preserving the patient from renewed attacks of bronchial catarrh.*

2d. *By preventing any inflammation that may exist, whether it be a catarrh, a pneumonia, a pleurisy, or what not, from extending to the pulmonary framework.*

3d. *By supporting, or at least not disturbing, the efficacy of the compensatory arrangements which have been developed without our assistance.*

Besides these main indications, others will of course arise from time to time; hemorrhages, putrid degeneration of bronchial secretions, etc., will make full demands upon our attention.

The *prophylaxis* of *bronchial catarrh* need not here be discussed exhaustively.

I will merely call attention to the fact that it is a mistake to stop cold washings, affusions, or rubbings, to which a patient is accustomed, during the continuance of a catarrh. If this is done, and the interruption lasts for a considerable time, it will be necessary gradually to accustom the patient to their use again.

After severe hemorrhages, on the other hand, I always have these applications stopped for at least a few days.

As there is generally no reason to fear the involvement of the lung structure until after the lapse of a considerable time from the beginning of a bronchial catarrh,—an acute catarrh but very exceptionally inducing this condition,—the thing to be prevented, above all else, is letting a bronchial catarrh *become chronic.*

I would not unduly depreciate the value of efforts in the direction of local treatment, but I do not believe that value to be high. We know how obstinate a well-rooted nasal or pharyngeal catarrh is likely to be, notwithstanding that both are far more accessible to local treatment than a catarrh of the bronchi, particularly of the finer ones. And this despite the best methods or apparatus for inhalation.

I lay the greatest stress upon the value of good local as well

as general nutrition, because we may, in this way, most readily create a power of resistance which will not permit the long continuance of newly acquired catarrhs as soon as external, injurious influences are avoided.

I hold the idea of Dr. Brehmer, of Görbersdorf, to be a correct and happy one, which proposes to improve the nutrition of the lungs through the appropriate regulation of the activity of the heart. We certainly need not limit its application to those cases of consumption which are characterized by defective power of the heart-muscle, whether this be congenital or acquired. On the contrary, I believe that Brehmer is quite correct in applying his views to the treatment of phthisis generally. I likewise see no reason why persons suffering from interstitial pneumonia, with a tendency to ever-recurring, long-continued catarrhs, should not be subjected to the same treatment. If it is successful in the graver conditions, we may, with greater confidence, expect that it will be so in those which are more trivial.

It may undoubtedly be accepted as the teaching of experience that pathological disturbances are sooner removed if the circulation of blood in the organs affected is active. This confirms the theoretical basis of Brehmer's procedures, the practical results of which are established beyond a doubt.

Brehmer himself has very correctly pointed out the importance of paying equal attention to the general as to the local nutrition. The composition of the blood depends essentially on the quality of the nutriment taken up. The nourishment of an individual organ depends as much upon the character of the blood as upon the amount which flows through that organ in a given period of time, therefore it likewise depends upon the nutritive material introduced.

The state of nutrition of a person suffering from habitual bronchial catarrh and bronchiectasis, or cirrhosis of the lungs, is liable to such great variations that no distinct "rules of living" can be laid down which would be always applicable. Any one familiar with the principles of scientific dietetics, as laid down in the works of Voit and his pupils, will readily hit on the right plan.

I would merely further remark that, in patients of this sort

more than in others, we must insist on proceeding slowly, and not causing a perhaps irremediable shattering of the constitution by too vigorous measures. A line of treatment, based on the laws of the metamorphosis of matter, calls for a firm and skilful hand in its application.

The value of certain baths has been empirically established. Even though we may be unable to tell the reason why, it is, nevertheless, true that Ems, Lippspringe, Ober-Salzbrunn, Soden, etc., have been of permanent benefit to many patients.

In the present state of our knowledge it is hardly possible, in any given case, to determine with certainty which will be more advantageous, a residence in Görbersdorf, in Davos, or at some other elevated spot, or at one of these baths. Every physician will refer to his own experience. Few will be in a position to deduce from this experience a definite scientific conclusion which would be accepted by others.

With this caution, I may express my own opinion that, as a general rule, those establishments situated at high altitudes, and in which Dr. Brehmer's ideas of treatment are carried out, are to be preferred.

But it is not every one whose circumstances will admit of his visiting a health resort. For the benefit of the large number who cannot do so, it will be well for us to carry out, as far as possible, the principles of Dr. Brehmer's treatment. No one will deny a certain supplementary value, in the way of treatment, to any method of exercise which induces deep inspirations, together with a degree of bodily activity that somewhat accelerates the pulse without making any excessive demands on the heart. This may be accomplished most satisfactorily by mountain climbing. The best way to secure conscientious obedience to our directions is to be very explicit in prescribing the number of inspirations to be taken in a minute, or the length of time that is to be spent in traversing a certain portion of road. I generally let my patients spend three or four hours a day in such exercise —not consecutive hours, and not the hours immediately following the principal meals of the day.

Considerable advantage may accrue from permitting patients to carry a stick laid across the back and under the arms, its extremities being grasped by the hands. This relieves the individual of the burden of his arms, and greatly facilitates the ex-

pansion of the chest. Such lung-gymnastics must take place in the open air.

One of the main requirements for persons suffering with chronic pulmonary troubles is an abundant supply of fresh, pure air. We do not mean to say that sleeping with open windows, and other similar extremes lately advocated with much bluster, are to be recommended to every one. Injurious air must certainly be avoided even at this price.

The *pneumatic treatment*, whether it be given in a cabinet or by means of a movable apparatus, the best of which is Waldenburg's, is sometimes of considerable value. In certain instances it succeeds in causing collapsed portions of lung to expand again, or overdistended portions to return to a smaller size. Nor would I underestimate the changes in the blood-distribution within the lungs, nor the influence on the amount of labor performed by the heart, which may be effected by this means. But I certainly doubt whether the expectations of Waldenburg [1] will be realized to their fullest extent.

I do not consider it necessary to restrict one's self to but one application a day of Waldenburg's apparatus. It has not appeared to me to be so powerful an agency. I have allowed three charges of the gasometer at a session to be used as often as six times a day without causing my patients any inconvenience.

There is one medicine which I give regularly and continuously —that is, oil of turpentine. All patients who continue to have an expectoration, even though it be but slight, after interstitial pneumonia, are ordered to take twenty to thirty drops of turpentine in milk every morning.

In support of this prescription I can only adduce my own experience. I believe I am safe in asserting that the amount of the expectoration is thereby diminished, its fetor is lessened or quite disappears, and in a short time a tolerance of the remedy is established which averts disturbances of the appetite or of digestion.

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[1] Die pneumatische Behandlung der Respirations- und Circulations-Krankheiten. Berlin: Hirschwald, 1875.

I direct the use of the turpentine to be continued from year to year.

In anæmic patients I prefer the use of arsenious acid, in doses of five milligrammes to one centigramme a day, rather than that of iron. It has appeared to me sometimes as if the entire condition had taken a turn for the better after the use of the arsenic.

In cirrhosis of the lungs the physiological compensation for the lost portions of respiratory surface is undertaken almost alone by the right side of the heart.

The efforts of this organ often suffice for a long period of time; but if the heart grows weak, then either bronchial catarrh follows, which readily becomes chronic, and is accompanied with renewed involvement of the lung-tissue, or all the manifestations arise which belong to cardiac insufficiency, as dropsy, etc.

I believe it to be important to keep all these things in mind when giving advice with regard to the manner of living of a person laboring under pulmonary cirrhosis. We shall then often be enabled to regulate matters which, while appearing trivial, may, in the long run, prove very important. I merely mention among these the use of tobacco, of spirituous drinks, the matter of keeping watch over the amount of fat accumulated in the body, the exercise of moderation in physical exertion, in singing, loud speaking, etc.

Our endeavor here must be, just as it is in valvular disease of the heart, to postpone as long as may be the period when it shall no longer be possible to provide adequate compensation; for it is a more than doubtful advantage to escape death by consumption or putrid bronchitis merely to perish through cardiac insufficiency.

There may come a time when all our therapeutic measures must be directed to combating this cardiac weakness. If the latter depends upon *actual degeneration of muscular tissue*, then all we can do is to afford temporary relief. This, however, is not the place to discuss the use of digitalis, of cardiac stimulants, etc.

The situation is quite different in case of *the deposit of fat within or upon the heart.* In my opinion, we may here generally

succeed, by means of appropriate diet, in effecting a gradual but *permanent* improvement.

We have still to consider the treatment of two incidental processes, viz. : *hemorrhage* and the *putrid degeneration of the bronchial secretion.*

I pointed out above how the pressure of blood effused and coagulated within the bronchial tubes may sometimes directly cause an opening into a vessel. In order that this can be accomplished, it is necessary that the blood should remain for a considerable time in contact with the place thus opened. Coughing is liable to cause its expulsion.

Any considerable distortion and distention of the bleeding vessel, such as must inevitably be caused by more violent respiratory movements, favors the detachment of a thrombus which forms in the interior of the vessel soon after the hemorrhage, plugging it up. Consequently, the suppression of violent respiratory movements is our first and most important duty.

Morphine, in doses not too small, fulfils this as well as another important indication.

A high degree of self-control or great habituation to the occurrence, is necessary to prevent a person who is having a pulmonary hemorrhage from becoming excited and having palpitation of the heart. The sudden and powerful increase of arterial tension certainly does not favor a cessation of the hemorrhage ; but if enough morphine is given to induce sleep, and by lowering reflex excitability to arrest cough, we have accomplished the first and most important thing to be done, viz. : to bring about conditions favorable to the arrest of the hemorrhage.

Objections to the use of opiates in pulmonary hemorrhages have recently been advanced from various sides. The basis of all of them, whether acknowledged or concealed, lies in Niemeyer's doctrine of the production of catarrhal pneumonia, or at least the favoring of pulmonary collapse, by means of the blood effused and left *in situ.* Even if we should admit the possibility of this taking place, it is still to be remarked that a person put to sleep with opium or morphine by no means breathes superficially, but deeply. Nor does he do this spasmodically, but quietly and uniformly, so that the distention of the vessels situ-

ated within the lung takes place gradually. If we compare with this the non-narcotized victim of a hemorrhage, noting his anxious, superficial respiration, observing how, on the slightest tendency to cough, his glottis closes, and the rapidly contracting abdominal muscles place the contents of the thorax under high pressure, we shall hardly remain in doubt that such a proceeding, while it maintains the hemorrhage, does nothing to prevent pulmonary collapse. On the contrary, the use of narcotics may be recommended to the adherents of Niemeyer, because *the quiet, deep sleep of morphine secures the expansion of the lung.*

The important point is not to give little doses, repeated every hour or two hours, by which the patient is never relieved from his state of excitement. I inject 1½ to 2 ctgm. (about ¼ to ⅓ of a grain) of morphine under the skin. At the end of half an hour at the outside the patient is usually asleep, his cough subsides, and his pulse grows quiet. On his awaking I repeat the dose if there is much tendency to cough. The mental excitement is not likely to continue unless the hemorrhage recurs.

As soon as the seat of the hemorrhage is known, it is well to employ the external application of cold. In common with most physicians, I apply large ice-bags.

In the way of nourishment I allow my patients for a few days only to take a little milk ; if they are very thirsty, to suck pieces of ice. It is, furthermore, essential to secure absolute rest in a comfortable position in bed, the head and shoulders being raised to facilitate the breathing, and to provide for the admission of fresh air.

This method of procedure has, at least, given me as good results as any other method recommended. It has this advantage over some of the others, that, inasmuch as it follows the physiological conditions found to exist, it can be intelligently and easily adapted to altered conditions as occasion may require.

Circumstances may demand a deviation from the procedures above described.

Some people, though not many, are utterly intolerant of morphine. They cannot be carried beyond the stage of excitement

which generally precedes narcosis. With such persons the remedy is to be avoided. At all events, no attempt should be made to compel rest by increasing the dose.

Sometimes we may then attain our purpose by the use of hydrate of chloral. But this also may fail, and, it appears to me, oftener than morphine. Under such circumstances I have once seen the excitement caused by chloral positively dangerous to life.

As a rule, we shall be spared all embarrassment, as the majority of patients have already at some time taken morphine and know how it acts with them.

Others find it difficult to remain in bed, as it causes a sense of constriction and cough. In such cases I have not been arbitrary, but have consented to their exchanging the bed for a comfortable seat.

Severe hemorrhages threatening life, under some circumstances, call for the employment of cardiac stimulants, or even of transfusion. Then the origin of the hemorrhage is of far less consequence than its amount, and all those rules hold good which are laid down for treatment in any case of serious loss of blood.

I make no use of the hæmostatic remedies of the books, as I have not been able to satisfy myself of their efficacy, and am convinced of their injurious effects whenever they are given in large quantities.

The putrid decomposition of the bronchial secretion, which attains a considerable extent and attacks healthy lung-tissue, demands careful treatment.

According to the communications of Gerhardt,[1] the methodical compression introduced by him, which produces forcible expiratory movements, seems, to a great degree, to effect the evacuation of the putrescent bronchial secretion which has been hoarded up. The employment of this compression twice a day was followed in a short time not only by rapid abatement of fever, but by the improvement of all the symptoms. I shall not hesitate, in the next case that comes under my treatment, to follow Gerhardt's method.

[1] D. Archiv f. klin. Med., Bd. XV., p. 1 et seq.

In these conditions also I should place the oil of turpentine at the head of the list of medicinal agents.

Under its use I have seen a cure effected in two cases of putrid bronchitis which attacked hitherto sound lungs, and ran a very severe course,—the lung-tissue in the one case being very deeply involved. This man died a little later from intestinal obstruction due to twisting of the gut, and post-mortem examination showed that the healing of the cavities then developed was already completed.

I give the remedy in large doses—ten to fifteen drops every two to three hours—and believe that we accomplish at least as much in this way as by inhalations, which are more inconvenient, are often very awkwardly carried out, and do not admit of any accuracy in the dose. I have some doubts about the advantages of the immediate action of turpentine upon a mucous membrane, inasmuch as when administered internally it reaches the bronchi in a greatly altered condition, having undergone chemical changes. There can be no question about its value when administered internally. When given by inhalation it is impossible to determine whether its efficacy is due to the contact of the unchanged oil with the mucous membrane or to the secondary action of the article as altered and found in the blood. I have never given more than a daily allowance of from 4 to 5 grammes, and have generally got along with from two to three. I have never seen any ill effects from the larger doses.

One of the most important indications in the treatment of putrid infection is to keep up the strength.

Besides combating the fever—the means for the accomplishment of which I need not here indicate—I lay great stress upon the liberal administration of alcohol, whether it be in the form of wine or of stronger liquors. I am of the opinion that this is the group of fevers above all others best adapted to the alcohol treatment for fever proposed by some. At the same time I have no experience in the exclusive employment of this method of treatment.

Ventilation cannot be strongly enough insisted upon.

Sometimes this cannot be sufficiently accomplished, even under the most favorable social conditions. I have had the bed of one of my patients placed in the middle of a hall, have had the

windows set open, in spite of severe cold weather, at the same time heating the room up as well as possible, and even then have not succeeded in entirely banishing the stench.

As soon as the weather will at all permit, it is well to bring such patients out into the open air, protecting them against the sun by means of a light canvas awning, or something of the kind.

This procedure has been tested at Kiel under such varied circumstances, and to so great an extent, and found unobjectionable, that I have entirely lost my fear that patients thus treated may "take cold."

INDEX.

Abdomen, passage of gall-stones into, 734.

Abdominal cavity, bile in, 658; opening of hepatic abscess into, 137.

Abdominal support in treatment of floating liver, 57.

Abscess, biliary, communicating with bronchi, 544; biliary, in contradistinction from hepatic, 547; embolic, hepatic, 93; hepatic, 88; hepatic, artificial opening of, 158; hepatic, as a complication of catarrh of the bile-ducts, 524; hepatic, in etiology of pylethrombosis, 789; hepatic, with cirrhosis of the liver, 200; idiopathic, of liver, 615, 824; multiple, hepatic, 836; of the brain, metastic, in interstitial pneumonia, 876; of the liver, 398.

Abscess formation in the liver, 560; in consequence of cholangitis, 548.

Acholia in explanation of the brain symptoms in acute atrophy of the liver, 284.

Acid, arsenious, in interstitial pneumonia, 911; benzoic, in acute atrophy of the liver, 305; carbolic, in hepatic abscess, 163; gallic, salts of, in the treatment of gall-stones, 774.

Acids, acetic and citric, in cholelithiasis, 776; biliary, and their salts, 697; biliary, influence of, in producing brain symptoms, 282; fatty, in expectoration of bronchiectasis, 894; fatty, in gall-stones, 697; in catarrh of the bile-ducts, 530; in hyperæmia of the liver, 78; in the treatment of gall-stones, 774.

Acini of the liver, 6.

Aconite in acute atrophy of the liver, 305.

Acute infectious diseases, in etiology of acute atrophy of the liver, 246; in etiology of cirrhosis of the liver, 171.

Adeno-carcinoma of the liver, 397.

Adenoma of the liver, 322, 350; diffuse, 397.

Affusions, cold, in interstitial pneumonia, 907.

Age, in etiology of amyloid degeneration of the liver, 416; in etiology of bronchiectasis, 863; in etiology of cancer of the biliary passages, 573; in etiology of cancer of the liver, 363; in purulent cholecystitis, 541; in the etiology of gall-stones, 706.

Air-passages, biliary fistula, communicating with, 663.

Albumen in the urine in acute atrophy of the liver, 275.

Albuminoids, putrefaction of, in bronchiectasis, 894.

Alcohol, in etiology of acute atrophy of the liver, 245; in etiology of cirrhosis of the liver, 168; in etiology of hepatic abscess, 108, 112; in etiology of hyperæmia of the liver, 61; in etiology of hypertrophic cirrhosis of the liver, 221; in putrid bronchitis, 915.

Alcoholics in suppurative hepatitis, 157.

Alimentary canal, condition of, in interstitial pneumonia, 872.

Alkalies, carbonated, in cirrhosis of the liver, 207; in catarrh of the bile-ducts, 530; in the treatment of gall-stones, 774; sulphates and tartrates of, in hepatic congestion, 79.

Aloes, in cirrhosis of the liver, 207; in hepatic congestion, 79; in suppurative hepatitis, 157.

Ammonia, hydrochlorate of, in suppurative hepatitis, 155.

Ammonium, chloride of, in amyloid degeneration of the liver, 438.

Amyloid degeneration of the liver, 407; nature, 409; etiology, 412; pathological anatomy, 417; pathology, 428; general picture of the disease, 429; symptoms, 430; diagnosis, 433; duration, termination, and prognosis, 435; therapeutics, 437; differential diagnosis from cirrhosis, 203.

Analysis, chemical, of expectoration in bronchiectasis, 894.

Aneurism, in etiology of compression of the gall-duct, 593; in etiology of perforations of the biliary passages, 652; of the hepatic artery, 834.

Angiocholitis, 534.

Anthelmintics in parasites of the biliary passages, 675, 682.

Antimony, tartarized, in suppurative hepatitis, 155.
Antiphlogistic measures in perforation of the biliary passages, 656.
Antiphlogosis, local and general, in exudative inflammation of the biliary passages, 556.
Appendix vermiformis, perforation of, in etiology of hepatic abscess, 95.
Aqua regia in suppurative hepatitis, 157.
Arsenic-poisoning, jaundice in, 28.
Arteria hepatica, embolism of, in etiology of hepatic abscess, 97.
Arteries, atheromatous degeneration of, with gall-stones, 712.
Artery, hepatic, aneurism of, 834; pulmonary, change in position of, in interstitial pneumonia, 882.
Ascaris lumbricoides in the biliary passages, 675.
Ascites, a sequel of cancer of the liver, 377; in chronic hepatic congestion, 73; in cirrhosis of the liver, 189; in interstitial pneumonia, 872; in pylethrombosis, 798; in syphilitic hepatitis, 233.
Astringents in suppurative hepatitis, 157.
Atelectasis of lungs in etiology of hemorrhage from the liver, 83.
Atheroma associated with gall-stones, 712.
Atrophy, acute, of liver, 238; anatomical changes in, 250; pathology of, 248; chronic, of the liver, in etiology of pylethrombosis, 789; cyanotic, of the liver, 67; cyanotic and induration of the liver, 203; granular, of the liver, 166; simple, of the liver, 202, 395.
Auscultation in perihepatitis, 185.

Bacteria, in acute atrophy of the liver, 258; in destruction of gall-stones, 705; globular, in etiology of hepatic abscess, 104.
Baths, in hyperæmia of the liver, 78; in interstitial pneumonia, 909; warm, in hepatic colic, 768; in suppurative hepatitis, 156.
Beer in cirrhosis of the liver, 207.
Belladonna in hepatic colic, 767.
Bile, accumulation of, in etiology of dilatation of the gall-bladder, 634; accumulation of, in the interval between periods of digestion, 508; amount and quality of, in fatty liver, 465; acid, in etiology of gall-stones, 702; changes in, in dilated ducts, 597; coloring matter of, 8; constitution of, in dilatation of the gall-bladder, 636; effect produced on the peritoneum by, 658; encapsulated exudation of, 654; in etiology of catarrh of the bile-ducts, 515; in the abdominal cavity, 658; method of passage of, into the circulation, 18; movement of, in the biliary passages, 506; place of origin of, 7; proportion of coloring matters in, 697; quantity secreted, 9, 509; site of absorption of, 509; site of secretion of, 509; stasis and retention of, 578.
Bile-ducts, abscesses in connection with, 547; anatomo-physiological remarks concerning, 500; calcification of the walls of, 549; cancer of, symptoms and diagnosis, 574; duration and treatment, 576; etiology of, 572; capillary, 7; catarrhal inflammation of, 509; symptomatology, 520; catarrh of, in etiology of gall-stones, 714; changes in, caused by tuberculosis, 566; changes in the bile in dilated, 597; chronic blennorrhœa of, 824; circulatory disturbances in the liver in etiology of catarrh of, 514; closure of, by biliary calculi, 824; complications and sequelæ of catarrhal inflammation of, 524; congenital occlusion of, 588; connective-tissue thickening of the walls of, 549; croupous inflammation of, 549; croup of, 557; diagnosis of catarrhal inflammation of, 525; dilatation of, 649; dilatation of, as a sequel of catarrh of, 524; diphtheritic inflammation of, 549; diseases of, 499; disorders in the canalization of the, 576; disturbances in the continuity of, 650; dropsy of, 597; duration, termination, and prognosis of catarrh of, 527; echinococcus in, 683; etiology of catarrhal inflammation of, 511; foreign bodies in etiology of stenosis of, 580; hemorrhage of, 561; inflammation of, in etiology of stenosis and occlusion of, 583; intra-hepatic, ulceration of, in etiology of hepatic abscess, 92; liver-leeches in, 670; muscular elements in, 505; neoplasms and tumors in etiology of stenosis and occlusion of, 589; occlusion of, by echinococcus, 581; occlusion of, in etiology of purulent and ulcerative inflammation, 539; parasites of, 669; parasites in etiology of stenosis and occlusion of, 581; pathological anatomy of catarrhal inflammation of, 515; pathology of catarrhal inflammation of, 518; perforation of, 651; perforations of, pathology and etiology of, 651; perforation of, symptoms and diagnosis of, 654; perforations of, terminations and prognosis and treatment of, 655, 656; peritonitis from perforation of, 555; persistent occlusion of, differential diagnosis from cirrhosis of the liver, 203; phlegmonous inflammation of, 549; poisons in etiology of catarrh of, 514.
Biliary colic, 744; fistulæ, 659; tumor, 633.
Biliary Passages, Purulent, Diphtheritic, and Exudative Inflammation of, 534; etiology, 536; pathological anatomy, 541; symptoms, 550; diagnosis, 553; duration, course, termination, 554; prognosis 555; treatment, 556; round-worm in, 675; rupture of, 656; rupture from dilatation, 598; stenosis of, 549, 577; stenosis and occlusion of, 578.
Biliary Passages, Stenosis and Occlusion of, 595; pathological anatomy, 595; pathology and general clinical history, 601; symptoms,

603; diagnosis, 613; causes, termination, and duration, 626; prognosis, 629; treatment, 630; treatment of catarrh of, 529; tumors of, 566; tumors in the region of, 566; ulcerative perforation of, 549; wounds of, followed by phlegmon, 540.

Biliprasin in the urine in cancer of the liver, 386.

Bilirubin, 8.

Blennorrhœa of the bile-ducts, 524; chronic, of the biliary passages, 824.

Blisters in hyperæmia of the liver, 82; in perihepatitis, 87.

Blood, abdominal supply of, affecting the liver, 4; anatomical changes in, in acute atrophy of the liver, 261; changed condition of, in etiology of hepatic abscess, 103; changes in, in cancer of the liver, 388; character of, during life, in acute atrophy of the liver, 270; local abstraction of, in exudative inflammation of the biliary passages, 556; local abstraction of, in hepatitis, 153; phenomena produced by biliary acids in, 23.

Bloodletting, in cirrhosis of the liver, 207; local, in hyperæmia of the liver, 81; local, in perihepatitis, 87.

Blood-vessels, anatomical changes in, in acute atrophy of the liver, 257; fatty degeneration of, in etiology of hemorrhage of the liver, 84; hepatic dilatation of, in etiology of hyperæmia of the liver, 59; hepatic, embolism of, in etiology of hepatic abscess, 92; hepatic, paralytic dilatation of, in etiology of hyperæmia of the liver, 62; in cancer of the liver, 340; rupture of, in etiology of hemorrhage of the biliary passages, 564.

Bone, suppuration of, in etiology of hepatic abscess, 99.

Bones, coloring matter of bile in, 20; suppuration and ulceration of, in etiology of waxy liver, 412.

Bowels, displacement of liver produced by inflation of, 47.

Brain, affections of, in cirrhosis of the liver, 199; affection of, in jaundice, 23; appearance of, in acute atrophy of the liver, 262; disturbances of, in suppurative hepatitis, 130; metastatic abscess of, in interstitial pneumonia, 876; symptoms, immediate cause of, in acute atrophy of the liver, 282.

Bronchi, communication of biliary abscess with, 544; inflammation of the connective tissue, in etiology of dilatation of, 862; opening of hepatic abscess into, 135.

Bronchial dilatations, forms of, 865.

Bronchiectases, interstitial pneumonia about, 861; situation of, 870.

Bronchiectasis, 837; pleurisy associated with, 862; pressure exerted by a column of air in respiration in etiology of, 859.

Bronchitis, putrid, 905; putrid, alcohol in, 915; putrid, oil of turpentine in, 915; and emphysema in interstitial pneumonia, 876; with cirrhosis of the liver, 201.

Buckthorn, bark of, in hyperæmia of the liver, 79.

CACHECTIC FATTY LIVER, 448.

Cachexia in etiology of fatty liver, 448; in etiology of hepatic abscess, 97; malarial and mercurial, in etiology of amyloid degeneration of the liver, 414.

Cæcum, suppuration in the vicinity of, in etiology of pylephlebitis, 809.

Calcification of the walls of the bile-ducts, 549.

Calculi, biliary, chronic obliteration of gall-ducts by, 397; closure of bile-ducts by, 824; in etiology of hepatic abscess, 92; in etiology of jaundice, 14.

Calomel in acute hepatitis, 154; in hepatic colic, 770; in hepatic congestion, 80; in perihepatitis, 87.

Canalization of the biliary passages, disturbances in, 576.

Cancer, granite-like, of the liver, 347; in etiology of hemorrhage of the liver, 83; in the region of the bile-ducts, 566; of the biliary passages, 566; of the gall-bladder, 640; of the hepatic veins, 834; clinical aspects of, 359; differential diagnosis from cirrhosis, 203; geographical distribution of, 365; pathological anatomy, 321; symptoms and diagnosis of, 368; of the portal vein, 826; with cirrhosis of the liver, 200.

Cancer-cells in the liver, 340.

Cancer-cicatrix in the liver, 336.

Carcinoma, in etiology of hemorrhage of the biliary passages, 564; in etiology of pylethrombosis, 789; telangiectodes of the liver, 337.

Cartilage, coloring matter of bile in, 20.

Castor-oil in acute hepatitis, 153.

Cataplasms, in acute perihepatitis, 87; in hyperæmia of the liver, 82; in suppurative hepatitis, 156.

Catarrh, in etiology of stenosis of the biliary passages, 584; bronchial, in etiology of bronchiectasis, 854; bronchial, in etiology of interstitial pneumonia, 850; bronchial, prophylaxis of, 907.

Cathartics, drastic, in cirrhosis of the liver, 209; saline, in exudative inflammation of the biliary passages, 556; in hepatic congestion, 78, 82.

Cells, epithelial and glandular, coloring matter of bile in, 20; hepatic, 6.

Chalybeates in suppurative hepatitis, 157.

Chloral, hydrate of, in pulmonary hemorrhage, 914.

Chloroform, as a lithontripticum, 773; in hepatic colic, 767.

Cholæmia, 10, 522; hematogenous, 24; hematogenous, symptoms of, 28; hepatogenous, 11, 12; hepatogenous, etiology of, 12.

Cholangioitis, 524, 557; catarrhalis, 509; hemorrhagic, 562.

Cholangitis, 534; spontaneous, 541; ulcerative, 651.
Cholecystitis, 557; contusions in etiology of, 540; hemorrhage in, 551; jaundice as a symptom of, 552; operative procedure in, 556; purulent, age in, 541; sex in, 541.
Cholecystotomy in dilatation of the gall-bladder, 647.
Cholelithiasis, 686; with cirrhosis of the liver, 200.
Cholepyrrhin, 694.
Cholera, in etiology of catarrh of the bile-ducts, 514; in etiology of cirrhosis of the liver, 170, 221; in etiology of hyperæmia of the liver, 63.
Cholesterine, 695, 696; gall-stones containing, 698; in etiology of gall-stones, 701.
Circulation, method of passage of bile into, 18; permanent impairment of, in the etiology of simple atrophy of the liver, 306.
Cirrhosis, annular, of the liver, 212; fœtal, of liver, 175; hypertrophic, of the liver, 217; in etiology of pylethrombosis, 789; insular, of the liver, 212; monolobular, of the liver, 212; multilobular, of the liver, 212; of the liver, 166, 398; anatomical changes in, 177; course, modes of termination, and prognosis in, 204; diagnosis of, 201; differential diagnosis from cyanotic induration, 68; etiology of, 168; in etiology of acute atrophy of the liver, 245; pathology of, 175; symptoms, 183; treatment of, 206.
Cirrhosis of the lungs, 837.
Cirrhotic crackling in interstitial pneumonia, 884.
Climate, change of, in etiology of hyperæmia of the liver, 62; in etiology of gall-stones, 709.
Cod-liver oil contraindicated in fatty liver of consumption, 472.
Coffee in etiology of hyperæmia of the liver, 61.
Cold, exposure to, in etiology of catarrh of the bile-ducts, 512; exposure to, in etiology of hepatic abscess, 91; in acute hepatitis, 153; in etiology of hepatic abscess, 112; in hemorrhage of the liver, 84; in hepatic congestion, 81, 82; in perihepatitis, 87; use of, in pulmonary hemorrhage, 913.
Colic, hepatic, 686, 741.
Colon, opening of hepatic abscess into, 134; passage of gall stones into, 730.
Coloring matter, biliary, 696.
Compression, methodical, in putrid bronchitis, 914.
Condition, social, in etiology of gall-stones, 710.
Connective tissue, coloring matter of bile in, 20; contraction of cicatricial, in etiology of bronchiectasis, 860.
Contusions in etiology of cholecystitis, 540.
Convulsions as a symptom in hepatic colic, 746; in acute atrophy of the liver, 277.
Copaiba, balsam of, in cirrhosis of the liver, 208.
Corpulence in etiology of gall-stones, 712; in etiology of hyperæmia of the liver, 60.
Cough, peculiarity of, in bronchiectasis, 892.
Counterirritation in exudative inflammation of the biliary passages, 556.
Craquement in interstitial pneumonia, 885.
Creasote in hepatic abscess, 153.
Croup of the biliary passages, 557.
Cupping in acute hepatitis, 153; in hyperæmia of the liver, 81.
Cyanosis in interstitial pneumonia, 873.
Cystic duct, congenital occlusion of, 588.
Cysticercus cellulosæ in the liver, 492.
Cysts from occlusion of the bile-ducts, 649.

Degeneration, acute fatty, of liver of the new-born, 455; amyloid, of liver, 203; calcareous, in dilated bronchi, 869; fatty, of the liver, 440; trabecular, of the bronchial wall, 870.
Diabetes mellitus, hypertrophy of the liver in, 315; in etiology of hyperæmia of the liver, 63; with cirrhosis of the liver, 200.
Diaphragm, acceleration or retardation of movements of, in etiology of jaundice, 16.
Diarrhœa in pylephlebitis, 819; in syphilitic hepatitis, 233.
Diathesis, hemorrhagic, in cancer of the liver, 404; in etiology of gall-stones, 711.
Diet, a faulty, in etiology of gall-stones, 713; in etiology of abscess of the liver, 108.
Dietetics in etiology of hyperæmia of the liver, 59.
Digestion, disturbances of, in chronic jaundice, 605; disturbance of, in fatty liver, 467.
Digestive canal, changes in mucous membrane of, in acute atrophy of the liver, 260.
Digitalis in acute hepatitis, 155; in cirrhosis of the liver, 208; in hepatic congestion, 78, 82.
Dilatation, simple, of the gall-bladder, 632.
Dilatations, forms of bronchial, 865.
Diphtheria, intestinal, in cirrhosis of the liver, 201.
Distoma hepaticum and distoma lanceolatum, 670; hæmatobium, 832.
Distomata in the portal vein, 832.
Diuretics, in cirrhosis of the liver, 208; in hyperæmia of the liver, 82.
Douches, cold, in cirrhosis of the liver, 207.
Dropsy of the biliary passages, 597; of the gall-bladder, 635, 636, 641.
Ducts, hepatic, gall-stones in, 743, 753.
Ductus choledochus, catarrhal swelling of, in etiology of cholæmia, 12; closure of, in etiology of hepatic abscess, 92; morbid conditions of, in etiology of interstitial hepatitis, 214; mucous membrane of and glands of, and muscular elements of, 504.
Ductus hepaticus, ulceration of, in etiology of hepatic abscess, 92.
Ductus Wirsungianus, dilatation of, in etiology of stenosis and occlusion of the biliary passages, 592.

Duodenum, cancer of, in etiology of stenosis and occlusion of the biliary passages, 591; catarrh of, in etiology of catarrh of the bile-ducts, 511; infiltration of substance of, in etiology of jaundice, 13; opening of hepatic abscess into, 134; passage of gall-stones into, 729.
Durande's remedy as a lithontripticum, 772.
Dust-lungs, 849.
Dysentery in etiology of hepatic abscess, 95, 109.

Echinococcus, hydatid thrill of, 639; in etiology of obstruction of the biliary passages, 581; in the biliary passages, 683; multilocular, of the liver, 399, 486; of the liver, 483, 487; of the liver, prognosis of, 490; of liver, therapeutics of, 491; sacs, in etiology of perforation of the biliary passages, 652.
Effusions, pleuritic, in etiology of interstitial pneumonia, 857.
Electricity in the treatment of gall-stones, 774.
Embolism by way of the hepatic vein, in etiology of hepatic abscess, 100; in etiology of hepatic abscess, 92; of arteria hepatica, in etiology of hepatic abscess, 97.
Embolus, refluent, 101.
Emetics, in catarrh of the bile-ducts, 530; in engorgement of the liver, 154; in hepatic colic, 770.
Emphysema and bronchitis in interstitial pneumonia, 876; pulmonary, with cirrhosis of the liver, 200.
Empyema, affection of upper portion of liver in, 3; in cancer of the liver, 393; of the gall-bladder, 545. 636, 641.
Endocarditis ulcerosa, in etiology of hepatic abscess, 97.
Endothelioma, primary melanotic, of the liver, 344.
Environment and occupation in etiology of bronchiectasis, 864.
Erysipelas capitis, in hepatic abscess, 140; in cirrhosis of the liver, 201; in etiology of jaundice, 13.
Ether as a lithontripticum, 773.
Excoriations in etiology of stenosis of the biliary passages, 584.
Exercise in hyperæmia of the liver, 78.
Expectorants, irritant, in perforation of hepatic abscess into the lungs, 164.
Expectoration, character of, in bronchiectasis, 891.
Extravasations of blood in acute atrophy of the liver, 261.
Exudation of encapsulated bile, 654.
Exudations, inflammatory, in etiology of displacement of the liver, 45.

Fæcal accumulations in etiology of retention-jaundice, 594.
Fæces, changes in, in cancer of the liver, 392.
Faradization of the gall-bladder in catarrh of the bile-ducts, 531.
Fasting, prolonged, condition of the gall-bladder in, 508.
Fat, amount of, in the ingesta in etiology of fatty liver, 444; in acute atrophy of the liver, 258; in the stools in chronic jaundice, 606.
Fatty Liver, 439; etiology, 444; frequency, 456; pathological anatomy, 457; pathology, 462; symptoms, 466; diagnosis, 468; duration, termination, and prognosis, 469; therapeutics, 470.
Fegato ambulante, 48.
Fever, intermittent hepatic, 754; intermittent, in etiology of cirrhosis of the liver, 170; intermittent, mistaken for pylephlebitis, 824; regular intermittent, in suppurative hepatitis, 127; typhoid, in etiology of interstitial pneumonia, 857.
Fevers, malarial, in etiology of hemorrhage of the liver, 83; malarial, in etiology of hyperæmia of the liver, 63.
Fibro-sarcoma of the liver, 354.
Fistulæ, abdominal, passage of gall-stones through, 735; between the biliary passages and the air-passages, 663; biliary, 659; biliary, diagnosis and prognosis of, 666; biliary, treatment of, 668; biliary, which empty into the urinary passages, 662; cutaneous biliary, 664; gastro-intestinal biliary, 660; vascular biliary, 663.
Floating liver, 48.
Foci, purulent and gangrenous, in etiology of perforation of the biliary passages, 651, 652.
Fœtus, condition of, in acute atrophy of the liver in the mother, 268.
Foreign bodies in etiology of gall-stones, 715; in etiology of perforations of the biliary passages, 651; in etiology of stenosis of the biliary ducts, 580; in the portal vein, 832.

Gall-bladder, accumulation of bile in, in etiology of dilatation of, 634; anatomical changes in, in acute atrophy of the liver, 257; cancer of, 570; catarrh of, in etiology of gall-stones, 714; chronic phlegmonous inflammation of, 720; concretions in, 718; constitution of the bile in dilatation of, 636; croupous and diphtheritic inflammation of, 542; dilatation of, 632; dilatation of, course, duration, termination, prognosis, 642; dilatation of, symptoms and diagnosis, 638; dilatation of, treatment of, 645; dropsy of, 635, 636, 641; empyema of, 545, 637, 641; faradization and compression of, in catarrh of the bile-ducts, 531; gall-stones in etiology of dilatation of, 634; gangrene of, 544; inflammation of, 541; mucous membrane of, 505; myxoma of, 568; phlegmonous inflammation of, 545; polypoid growths of, 567; rupture

from dilatation, 598; traumatism in etiology of dilatation of, 634; ulcers of, 542.
Gall-ducts, chronic obliteration of, 397; dilated, in etiology of hepatic abscess, 92; interstitial hepatitis from affections of, 213; purulent inflammation of, 546; ulcers of, 546.
Gall-stones, 686; as a sequel of catarrh of the bile-ducts, 524; atheromatous degeneration of the arteries with, 712; changes in, in the intestinal canal, 738; chemical composition of, 696; compound nucleated, 694; containing cholesterine, 698; course, terminations, and prognosis of, 764; destitute of cholesterine, 699; diagnosis of, 759; etiology of, 706; expulsion of, by vomiting, 739; formation within the liver, in etiology of interstitial hepatitis, 213; impaction of, in the intestine, 739; in etiology of catarrh of the bile-ducts, 515; in etiology of dilatation of the gall-bladder, 634; in etiology of occlusion of the biliary ducts, 580; in etiology of purulent, diphtheritic, and ulcerative inflammation of the bile-ducts, 536; in the portal vein, 832; mode of origin of, 700; passage of, into the abdominal cavity, 734; passage of, into the colon, 730; passage of, into the duodenum, 729; passage of, into the portal vein, 731; passage of, into the stomach, 729; passage of, into the urinary passages, 730; passage of, through abdominal fistulæ, 735; pathology and pathological anatomy of, 715; physical characteristics of, 690; simple homogeneous, 693; symptoms of, 742; the structure of, 693; treatment of, 766.
Gangrene of the gall-bladder, 544; of the intestine, 741.
Gastro-enteritis in etiology of hepatic abscess, 91; in etiology of jaundice, 13.
Glands, bronchial lymphatic, condition of, in bronchiectasis, 871; lymphatic, enlargement of, in etiology of obstruction of the biliary passages, 592; lymphatic, of the porta hepatica, condition of, in acute atrophy of the liver, 258.
Glisson's capsule, abscess in, in etiology of pylephlebitis, 812.
Glycin, 10.
Glycogen, formation of, 9.
Gout in etiology of cirrhosis of the liver, 172; in etiology of gall-stones, 711; in etiology of waxy liver, 714.
Gravel, biliary, 750.
Gravidity in etiology of acute atrophy of the liver, 244.

Habits, sedentary, in etiology of gall-stones, 713.
Heart, affections of, with cirrhosis of the liver, 200; affections of, in etiology of hyperæmia of the liver, 58; changes in muscular tissue in cirrhosis of the liver, 199; muscular tissue of, in acute atrophy of the liver, 260; paralytic condition of, in jaundice, 23; position of, in interstitial pneumonia, 882.
Hemorrhage, gastric and intestinal, in cirrhosis of the liver, 194; hepatic, 83; in cholecystitis, 551; of the biliary passages, 561; pulmonary, in interstitial pneumonia, 899; gastric and intestinal, in syphilitic hepatitis, 233; in acute atrophy of the liver, 270, 288; in chronic jaundice, 610; in stenosis and occlusion of the biliary passages, 602; pulmonary, use of ice-bags in, 913; pulmonary, morphine in, 912; pulmonary, in interstitial pneumonia, 889; pulmonary, etiology of, in interstitial pneumonia, 900; suppression of habitual, in etiology of hyperæmia of the liver, 63; warning, in interstitial pneumonia, 900.
Hemorrhoids, arrest of habitual hemorrhage from, in etiology of hepatic congestion, 64; in cancer of the liver, 392.
Hepar, migrans, 48.
Hepatic colic, 686.
Hepatic duct, gall-stones in, 717.
Hepatic vein, closure of, in etiology of cirrhosis of the liver, 172; embolism by way of, in etiology of hepatic abscess, 100.
Hepatitis, circumscribed syphilitic, 227; cytophthora, 238; diffusa parenchymatosa, 238; fibrosa, 166; interstitial, from affections of the gall-ducts, 213; interstitial, rarer forms of, 211; metastatic, symptoms of, 114; suppurative, 88, 550, 555; suppurative, anatomical changes in, 115; suppurative, complications, 139; suppurative, course, duration, termination, and prognosis of, 144; suppurative, diagnosis of, 140; suppurative, etiology of, 90; suppurative, general features of the disease, 113; suppurative, pathology, 113; suppurative, symptomatology, 121; suppurative, treatment of, 152; syphilitic, 222; syphilitic, pathology of, 224; etiology of, 223; syphilitic, symptomatology of, 231; tropical, fever in, 128; tropical, idiopathic character of, 129; vera, sive suppuratoria, 88.
Hepato-peritonitis, 84.
Heredity in etiology of cancer of the liver, 362; in etiology of gall-stones, 711; in etiology of hepatic congestion, 65.
Histogenesis of cancer of the liver, 341.
Hydatids of the liver, 399.
Hydrops ductum biliarum saccatus, 597.
Hyperæmia of the liver, 57.
Hyperplasia of the liver, 314.
Hypertrophy of the liver, 313; compensatory, 314.
Hypochondriasis in chronic hepatic hyperæmia, 73.
Hypochondrium, tension in the right, in hepatic congestion, 70.

Ichorrhæmia in etiology of hepatic abscess, 103.
Icterus, 10; catarrhalis, 509; menstrualis, 14, 18; neonatorum, 16, 614; spasticus, 15; vernalis and autumnalis, 512; viridis, 22.
Indican in the urine in cancer of the liver, 387.
Induration, cyanotic, of the liver, 68; granular, of the liver, 186; simple, of the liver, 212.
Infection, acute septic, in etiology of acute atrophy of the liver, 247.
Infectious diseases, acute, in etiology of inflammation of the bile-ducts, 537.
Infiltration, fatty, of the liver, 440.
Inhalations, antiseptic, in perforation of hepatic abscess into the lungs, 164.
Insomnia in suppurative hepatitis, 129.
Intellect, disorders of, in chronic hepatic hyperæmia, 73
Intestinal canal, changes in gall-stones in, 738.
Intestinal walls, gall-stones in etiology of ulceration, gangrene, and perforation of, 741.
Intestine, impaction of gall-stones in, 739; symptoms referable to, in cirrhosis of the liver, 192; ulceration, gangrene, and perforation of, 741.
Iodine in amyloid degeneration of the liver, 438; in chronic hepatic fistula, 164; in cirrhosis of the liver, 207; in hepatic abscess, 163; in perihepatitis, 87.
Iron in cirrhosis of the liver, 207; iodide of, in syphilitic hepatitis, 237; preparations of, in amyloid degeneration of the liver, 438; preparations of, in simple atrophy of the liver, 313.
Irritants, cutaneous, in hepatic congestion, 82.

Jaundice, 10; aneurism in etiology of, 593; as a symptom in abscess of the liver, 615; as a symptom in acute atrophy of the liver, 267; as a symptom in cancer of the biliary passages, 574; as a symptom in cancer of the liver, 384; as a symptom in occlusion of the biliary passages, 602, 603; as a symptom in stenosis of the bile-ducts, 582; as a symptom in syphilitic hepatitis, 233; as a symptom of catarrh of the bile-ducts, 510; as a symptom of cholecystitis, 552; calculi in etiology of, 14; catarrhal, 824; catarrhal, causes of, 511; cause of, in floating liver, 55; change in the position of the liver in etiology of, 594; chronic, condition of the glomeruli of the kidneys in, 608; chronic, condition of urine in, 607; chronic, constitution of stools in, 606; chronic, disturbances of digestion in, 605; chronic, hemorrhages in, 610; chronic, pulse in, 609; chronic, stearrhœa in, 606; chronic, treatment of pruritus in, 631; chronic, xanthopsia in, 609; epidemic, in etiology of acute atrophy of the liver, 248; epidemics and endemics of, 512; erysipelas in, etiology of, 13; form of, in pyæmic and puerperal fever, 13; from suppression, 26; hematogenous, 24; hematogenous, symptoms of, 28; hepatogenous, etiology of, 12; hepatogenous, general symptoms of, 19; hypertrophic cirrhosis with, 218; in acute atrophy of the liver, 260; in biliary colic, 748; in cirrhosis of the liver, 195; in hepatic congestion, 70; in purulent inflammation of the portal vein, 818; in suppurative hepatitis, 126; menstrual, 72; mode of origin of, in acute atrophy of the liver, 280; neoplasms in, etiology of, 14; phosphorus-poisoning in, etiology of, 14; symptomatic catarrhal, treatment of, 534.

Kidneys, affections of, etiology of hepatic congestion in, 65; anatomical changes in, in acute atrophy of the liver, 260; condition of, in bronchiectasis, 872; condition of the glomeruli of, in intense jaundice, 608; diseases of, with cirrhosis of the liver, 199; disturbances of, in jaundice, 22; opening of hepatic abscess into, 135; pathological condition of, in occlusion of the biliary passages, 601; tumors of the right, in etiology of obstruction of the biliary passages, 592.
Krasis, pyemic, in etiology of hepatic abscess, 103.

Labor, difficult, in etiology of hemorrhages of the liver, 83.
Laxatives, in catarrh of the bile-ducts, 533; in hepatic congestion, 79; in suppurative hepatitis, 157.
Leeches, in acute hepatitis, 153; in hyperæmia of the liver, 81; in perforative peritonitis, 656; liver, 670; to the anus in exudative inflammation of the biliary passages, 556.
Leptothrix buccalis in bronchiectasis, 893.
Leucæmia with cirrhosis of the liver, 200.
Leucæmic hepatic tumor, 315.
Leucin in acute atrophy of the liver, 258, 273.
Lithontripticum, Durande's, 772.
Liver, abscess of, 398; acute atrophy of, 238; acute atrophy of, anatomical changes in, 250; acute atrophy of, diagnosis, 298; acute atrophy of, duration, termination, prognosis, 301; treatment, 304; acute atrophy of, etiology of, 242; acute atrophy of, nature of the anatomical process, 290; acute atrophy of, pathology of, 248; acute atrophy, symptomatology, 262; acute fatty degeneration of the new-born, 455; acute phosphorus-poisoning in etiology of, 454; adenoma of, 322, 350; amount and quality of bile in fatty, 465; amyloid degeneration of, 407; analysis of the prominent symptoms of acute atrophy of, 279; anatomical changes in hyperæmia of, 66; cachexia in etiology of fatty, 448; cancer of, clinical aspects of, 359; cancer of, duration of, 401; cancer of, gastro-intestinal symptoms, 391; cancer of, pathological anatomy of, 321; cancer of, termina-

tion and prognosis of, 402; cancer of, treatment of, 404; change in position of, in etiology of retention-jaundice, 594; chronic atrophy of, in etiology of thrombosis of the portal vein, 789; cirrhosis of, 398; condition of, in bronchiectasis, 872; cyanotic, induration of, 68; development of pigmented, 479; diagnosis of amyloid degeneration of, 433; diagnosis of fatty, 468; diagnosis of hyperæmia of, 76; diffuse, adenoma of, 397; diffuse hyperplasia of, 314; diminution in size of, in acute atrophy, 262; diseased conditions of, in etiology of pylephlebitis, 811; duration, termination, and prognosis of amyloid degeneration of, 435; duration, termination, and prognosis of fatty, 469; dyscrasia of inebriety in etiology of fatty, 453; echinococcus of, 483; echinococcus, diagnosis of, 487; echinococcus of, prognosis of, 490; echinococcus of, therapeutics of, 491; fatty, 439; fatty, atrophy of, 455; fatty, etiology of, 444; fatty, nutmeg, 455; floating, diagnosis of, 55; floating, etiology of, 48; floating, symptoms of, 51; flukes, 670; flukes in etiology of stenosis of the bile-ducts, 582; frequency of fatty, 456; general picture of amyloid degeneration of, 429; geographical distribution of, 365; hemorrhage of, 83; hypertrophy of, 313; idiopathic abscess of, 824; microscopical examination of the melanæmic, 476; multiple adenoid tumors of, 397; nutmeg, 68; parasites of, 483; pathological anatomy of amyloid degeneration of, 417; pathological anatomy of fatty, 457; pathology of amyloid degeneration of, 428; pathology of fatty; 462; physical diagnosis of diseases of, 33; primary melanotic endothelioma of, 344; prognosis of pigmented, 480; rust-brown atrophic, 473; sarcoma of, 322, 353; simple atrophy of, 305; simple atrophy of, pathological anatomy, 307; suppurative inflammation of, 88; symptomatology of amyloid degeneration, 430; symptoms and diagnosis of cancer of, 368; symptoms of fatty, 466; symptoms of hyperæmia of, 69; syphilitic, 400; therapeutics of amyloid degeneration of, 437; therapeutics of fatty, 470; treatment of hyperæmia of, 77; therapeutics of pigmented, 480; wax-like, 459.

Lung-gymnastics in interstitial pneumonia, 910.

Lungs, cirrhosis of, 837; cold in perforation of hepatic abscess into, 164; affections of, in etiology of hyperæmia of the liver, 58; affections of, in hepatic abscess, 140; atelectasis of, in etiology of hemorrhage of the liver, 83.

Lymphatics, deep, of liver, 8; of liver, origin of, 19.

Lympho-sarcoma of the liver, 355.

Magnesia, citrate of, in acute hepatitis, 153.

Malaria, in etiology of cirrhosis of the liver, 170; in etiology of hyperæmia of the liver, 63.

Marasmus, in etiology of simple atrophy of the liver, 305; in etiology of thrombosis of the portal vein, 787.

Measles in the etiology of interstitial pneumonia, 856.

Mechanical treatment of catarrh of the bile-ducts, 531.

Mediastinum, displacement of, in interstitial pneumonia, 883; tumors of, in etiology of hyperæmia of the liver, 58.

Melanæmia, 474; anatomical conditions of the liver in, 476.

Melanæmic liver, 473.

Melano-sarcoma of the liver, 343.

Melanuria in cancer of the liver, 387.

Membranes, serous and fibrous, coloring-matter of bile in, 20.

Meningitis, epidemic cerebro-spinal, in etiology of hyperæmia of the liver, 63.

Menstruation, disorders of, in etiology of hyperæmia of the liver, 63.

Mental emotion depressing in etiology of acute atrophy of the liver, 245.

Mercurials in suppurative hepatitis, 157.

Mercury, in cirrhosis of the liver, 207; in syphilitic hepatitis, 238.

Mesentery, purulent deposit between the layers of, in etiology of pylephlebitis, 810.

Meteorismus in etiology of displacements of the liver, 47.

Miasma in etiology of acute atrophy of the liver, 247.

Micrococcus septicus in etiology of hepatic abscess, 103.

Milk contraindicated in fatty liver of consumptives, 472.

Morphine, in perihepatitis, 87; in pulmonary hemorrhages, 912.

Mucous membrane, bronchial, condition of, in bronchiectasis, 869.

Musk in acute atrophy of the liver, 305.

Mustard in etiology of hyperæmia of the liver, 61.

Myxoma, in the region of the bile-ducts, 566; of the gall-bladder, 568.

Myxo-sarcoma of the liver, 355.

Narcotics in suppurative hepatitis, 157.

Neoplasms, in etiology of amyloid degeneration of the liver, 414; in etiology of jaundice, 14; in etiology of perforations of the biliary passages, 652; in etiology of stenosis of the biliary passages, 589; of abdominal organs, in etiology of displacement of the liver, 45.

Nerves, paralysis of vaso-motor, in etiology of hyperæmia of the liver, 63.

Nervous system, derangements of, in acute atrophy of the liver, 276; disturbances of, in cirrhosis of the liver, 798; phenomena of, in jaundice, 23.

New-born, acute fatty degeneration of the liver in, 455.
Nutmeg liver, 68; atrophied, 69.
Nutrition, affection of, in suppurative hepatitis, 133; general, condition of, in cancer of the liver, 382.

Obstruction, prolonged intestinal, caused by impaction of gall-stones, 740.
Occlusion, congenital, of the biliary passages, 588; of the biliary excretory ducts, 578; of the portal vein, 785; permanent, as a sequel of catarrh of the bile-ducts, 524.
Ointment, mercurial, in syphilitic hepatitis, 238.
Opium, in hepatic colic, 766; in peritonitis, due to perforation of hepatic abscess into the abdominal cavity, 165; in peritonitis, from perforation of the biliary passages, 656; in suppurative hepatitis, 154, 157.
Osteosarcoma of the liver, 355.
Ovaries, suppurative processes in, in etiology of hepatic abscess, 96.

Pachymeningitis, chronic, in cirrhosis of the liver, 200.
Pain, as a symptom in cancer of the liver, 380.
Pancreas, tumors of, in etiology of occlusion of the biliary passages, 591.
Paracentesis, in chronic hyperæmia of the liver, 83; in cirrhosis of the liver, 210.
Parasites, in etiology of catarrh of the bile-ducts, 515; in etiology of purulent, diphtheritic, and ulcerative inflammation, and of catarrh of the bile-ducts, 537; in etiology of stenosis of the biliary passages, 581; of the biliary passages, 669; of the liver, 483; of the portal vein, 832.
Parenchyma, pulmonary, changes in, in bronchiectasis, 871.
Pars intestinalis choledochi, 504.
Pathogenesis of acute atrophy of the liver, 292.
Pentastomum denticulatum in the liver, 492.
Pepper, in etiology of hyperæmia of the liver, 61.
Perforation of the intestine, 741; ulcerative, of the bile-ducts, 549; of the biliary passages, 651.
Pericarditis, in cirrhosis of the liver, 201; in suppurative hepatitis, 132, 139.
Pericardium, abnormal contents, in etiology of displacement of the liver, 43; opening of hepatic abscess into, 137.
Perihepatitis, 84; anatomical changes in, 85; auscultation in diagnosis of, 185; chronic, differential diagnosis from cirrhosis, 201; differential diagnosis of, 86, 87; etiology of, 84; in etiology of stenosis of the biliary passages, 587; prognosis and treatment of, 87; symptoms of, 85.
Periphlebitis chronica hepatica, in etiology of hyperæmia of the liver, 58.
Peripylephlebitis syphilitica, 814.
Peritoneum, effect upon, produced by the bile, 658.
Peritonitis, chronic, cirrhosis of liver supplementary to, 173; chronic, in etiology of pylethrombosis, 790; chronic, in etiology of simple atrophy of the liver, 308; diffuse chronic, differential diagnosis from cirrhosis of liver, 202; from discharge of bile into the abdominal cavity, 653; from perforation of bile-ducts, 555; general, in suppurative hepatitis, 131; in cirrhosis of the liver, 201; in pylephlebitis, 819; localized purulent, in etiology of hepatic abscess, 96; with effusion, a sequel of cancer of the liver, 377.
Phlebitis, adhesiva hepatica, 833; purulenta hepatica, 833; umbilicalis, in etiology of hepatic abscess, 93.
Phlegmon, following wounds of the bile-ducts, 540.
Phosphorus-poisoning, in etiology of acute atrophy of the liver, 246, 296; in etiology of cirrhosis of the liver, 172; in etiology of catarrh of the bile-ducts, 514; in etiology of jaundice, 14; jaundice in, 28.
Phthisis, chronic pulmonary, in etiology of waxy liver, 413; pulmonary, in etiology of interstitial pneumonia, 855.
Physiognomy in cancer of the liver, 382.
Pigment Liver, 473; anatomical conditions and microscopical examination, 476; development of, 479; prognosis and therapeutics of, 480.
Pleura, abnormal contents of, etiology of displacement of liver, 43, 44; diseases of, in etiology of hyperæmia of the liver, 58; opening of hepatic abscess into, 136.
Pleurisy associated with bronchiectasis, 862.
Pleuritis, in suppurative hepatitis, 132, 139; with cancer of the liver, 393.
Pneumatic treatment of interstitial pneumonia, 910.
Pneumonia, catarrhal, in etiology of interstitial pneumonia, 853; croupous, in the etiology of interstitial pneumonia, 857; croupous, intercurrent in interstitial pneumonia, 876; in suppurative hepatitis, 139; interstitial, 837; interstitial, about bronchiectatic cavities, 861; interstitial diagnosis and prognosis, 902; interstitial, etiology of, 846; interstitial, general clinical history of, 873; interstitial, pathological anatomy of, 864; interstitial, pathology of, 872; interstitial, treatment of, 906; with cirrhosis of the liver, 201.
Podophyllin, in hepatic colic, 770; in hyperæmia of the liver, 80.
Poisons in etiology of catarrh of the bile-ducts, 514.
Polypi of the gall-bladder, 567.
Portal vein, closure of, in etiology of cirrhosis of the liver, 173; embolism of, in etiology of hepatic abscess, 92; hemorrhage from, in etiology of cholæmia, 17; obliteration of branches of, in

etiology of hyperæmia of the liver, 64; occlusion of, differential diagnosis from cirrhosis of liver, 202; perforation of, by hepatic abscess, 138; thrombosis of, in cirrhosis of the liver, 200; thrombosis of, in etiology of hepatic abscesses, 96.
Potash, acetate of, in hyperæmia of the liver, 82.
Potassium, iodide of, in syphilitic hepatitis, 237.
Pregnancy in etiology of acute atrophy of the liver, 244; in etiology of retention jaundice, 595.
Prolapsus ani, hepatic abscess following operations for, 95.
Pruritus in chronic jaundice, 631; treatment of, in jaundice, 533.
Psorosperms in the liver, 494.
Puerperal fever, form of jaundice in, 13; in etiology of acute atrophy of the liver, 246.
Pulse, diminution of the frequency of, in chronic jaundice, 609.
Puncture, explorative, in diagnosis of fluctuating tumor of the gall-bladder, 641; in dilatation of the gall-bladder, 646; in etiology of hyperæmia of the liver, 63.
Purgatives in acute hepatitis, 153.
Pyæmia, form of jaundice in, 13; hematogenous, jaundice in, 27; hepatic abscess in, 100; in etiology of purulent inflammation of the biliary passages, 537.
Pylephlebitis, 830; adhesiva, 792, 797; chronica, 398, 830; in etiology of cholæmia, 17; purulenta, 550, 555.
Pylethrombosis, 785; in etiology of cholæmia, 17.

Quinine in acute hepatitis, 155; in cirrhosis of the liver, 208; in exudative inflammation of the biliary passages, 557; in pigment liver, 480; in suppurative hepatitis, 157.

Rachitis, in etiology of displacement of the liver, 43; in etiology of waxy liver, 414.
Rectum, wounds of, in etiology of hepatic abscess, 95.
Rectus abdominalis muscle, tension of, in hepatic abscess, 123.
Recurrent fever in etiology of acute atrophy of the liver, 246.
Respiration, in interstitial pneumonia, 873; in the etiology of bronchiectasis, 842; variations of, in etiology of hyperæmia of the liver, 60.
Respiratory organs, abnormal appearances of, in hepatitis, 131.
Rest, in treatment of perihepatitis, 87; in treatment of suppurative hepatitis, 158.
Retina, hemorrhages into, in cirrhosis of the liver, 198.
Rhubarb in cirrhosis of the liver, 207; in hepatic congestion, 79; in suppurative hepatitis, 157.
Round-worm in the biliary passages, 675.
Rupture of the biliary passages, 656.

Salts, neutral, in hepatic congestion, 79; neutral, in perihepatitis, 87.
Sarcoma of the liver, 322, 353; radiated, of the liver, 349.
Scarlet fever in etiology of hyperæmia of the liver, 63.
Sclerosis, general, of the liver, 217.
Scurvy in etiology of hemorrhages of the liver, 83; in etiology of hyperæmia of the liver, 63.
Season of the year in etiology of gall-stones, 709.
Senna in suppurative hepatitis, 157.
Sex, in cholecystitis, 541; in etiology of amyloid degeneration of the liver, 417; in etiology of bronchiectasis, 864; in etiology of cancer of the biliary passages, 572; in etiology of cancer of the liver, 364; in etiology of gall-stones, 708; in frequency of occurrence in fatty liver, 456.
Shoulder, pain in, as a symptom in suppurative hepatitis, 125.
Sinapisms in hepatic colic, 768.
Singultus as a symptom in cancer of the liver, 394; in suppurative hepatitis, 132.
Skin, changes in, in cancer of the liver, 382; color of, in syphilitic hepatitis, 234; condition of, external, in fatty liver, 468; gangrene of, a complication of cirrhosis of the liver, 201.
Skull, wounds of, in etiology of hepatic abscess, 100.
Sleep, anomalies of, in suppurative hepatitis, 129.
Snake-bite, jaundice in, 28.
Soda, bicarbonate, in the treatment of gall-stones, 776; carbonate of, in hepatic congestion, 79; chlorate of, in cirrhosis of the liver, 207; muriate of, in hepatitis, 156; sulphate of, in acute hepatitis, 153; sulphate of, in hepatic congestion, 79; sulphate of, in the treatment of gall-stones, 776.
Soil, condition of, in etiology of gall-stones, 709.
Spices, irritant, in etiology of cirrhosis of the liver, 169; in etiology of hyperæmia of the liver, 61.
Spinal cord, affection of, in jaundice, 23.
Spleen, anatomical changes in, in acute atrophy of the liver, 261; changes in, in acute atrophy of the liver, 269; changes in, in cirrhosis of the liver, 188; changes in, in hypertrophic cirrhosis of the liver, 218; condition of, in bronchiectasis, 872; condition of, in cancer of the liver, 379; condition of, in purulent inflammation of the portal vein, 818; condition of, in suppurative hepatitis, 132; condition of, in syphilitic hepatitis, 234; purulent focus in, in etiology of pylephlebitis, 810; swelling of, in acute atrophy of the liver, 290.
Stearrhœa in chronic jaundice, 606.
Stenosis of the bile-ducts, 549; of the biliary excretory ducts, 578.

Stethoscope in diagnosis of diseases of the liver, 40.
Stimulants, cardiac, in pulmonary hemorrhage, 914; in hepatic colic, 769.
Stomach, distention of, in etiology of hyperæmia of the liver, 60; disturbances of, in hyperæmia of the liver, 72; disturbances of, in suppurative hepatitis, 130; opening of hepatic abscess into, 134; passage of gall-stones into the, 729; "spoiled" stomach in etiology of catarrh of the bile-ducts, 512; suppurative process in, in etiology of pylephlebitis, 810; symptoms referable to, in cirrhosis of the liver, 192.
Stools, constitution of, in chronic jaundice, 606.
Stricture, cicatricial, in etiology of stenosis of the biliary passages, 585.
Sugar in acute atrophy of the liver, 258.
Suppuration in etiology of amyloid degeneration of the liver, 412.
Sweat-glands, action of, in jaundice, 22.
Syphilis, constitutional, in etiology of waxy liver, 413; diffuse hepatic, 225; in etiology of cirrhosis of the liver, 169; in etiology of interstitial pneumonia, 835.
Syphilitic liver, 400.

Taste, abnormities of, in jaundice, 23.
Temperature, high atmospheric, in etiology of hyperæmia of the liver, 62.
Thrombosis, chronic, of the portal vein, 307; in etiology of hepatic abscess, 93; of the portal vein, 785; of portal vein, with cirrhosis of liver, 200.
Transudations, hemorrhagic, in cancer of the liver, 393; serous, in acute atrophy of the liver, 262.
Traumatism, in etiology of dilatation of the gall-bladder, 634; in etiology of hemorrhage of the liver, 83; in etiology of hyperæmia of the liver, 61; in etiology of pylephlebitis, 807; in etiology of rupture of the biliary passages, 656; in etiology of suppurative inflammation of the liver, 90.
Tuberculosis, changes in the bile-ducts caused by, 563; in etiology of interstitial pneumonia, 856.
Tumor, biliary, 545, 633.
Tumors, hydatid, of liver, 399; in etiology of pylethrombosis, 792; in etiology of stenosis of the biliary passages, 589; inflammatory, of the gall-bladder, 643; multiple adenoid, of liver, 397; of the biliary passages, 566.
Turpentine, ethereal spirits of, in cirrhosis of the liver, 209; oil of, in interstitial pneumonia, 910; oil of, in putrid bronchitis, 915.
Typhoid fever, in etiology of acute atrophy of the liver, 246; in etiology of catarrh of the bile-ducts, 514; in etiology of diphtheritic inflammation of the bile-ducts, 538; in etiology of hepatic abscess, 92; in etiology of hyperæmia of the liver, 63.
Typhus, in etiology of cirrhosis of the liver, 170; in etiology of hypertrophied cirrhosis of the liver, 221; jaundice in, 28; recurrens, in etiology of jaundice, 18; spotted, in etiology of hyperæmia of the liver, 63.
Tyrosin, in acute atrophy of the liver, 258, 273; in expectoration of bronchiectasis, 894.

Ulcer of mucous membrane of the gall-bladder, 542; of the stomach, in etiology of hepatic abscess, 94; of stomach, perforating, in etiology of hepatic abscess, 92.
Ulceration, in etiology of amyloid degeneration of the liver, 412; of the intestine, 741.
Ulcers, in etiology of hemorrhage of the biliary passages, 564; in etiology of stenosis of the biliary passages, 584; intestinal, in etiology of hepatic abscess, 95; of the gall-ducts, 546.
Uræmia in explanation of the brain symptoms in acute atrophy of the liver, 284.
Urea, diminution of, in intermittent hepatic fever, 756.
Urinary passages, passage of gall-stones into the, 730.
Urine, changes in, in acute atrophy of the liver, 273; changes in, in cirrhosis of the liver, 196; changes in, in jaundice, 21, 22; changes in, in pylethrombosis, 801; changes in, in suppurative hepatitis, 132; changes in, in syphilitic hepatitis, 234; condition of, in cancer of the liver, 386; condition of, in chronic jaundice, 607; condition of, in simple atrophy of the liver, 311; diminution in quantity of, in acute atrophy of the liver, 287.
Uterus, suppurative processes in, in etiology of hepatic abscess, 96.

Vein, portal, anatomical and physiological remarks concerning the, 779; calcification and ossification of, 830; cancer of, 826; course, duration, terminations, and prognosis of purulent inflammation of, 825; course, duration, terminations, and prognosis of thrombosis and occlusion of, 803; diagnosis of purulent inflammation of, 822; diagnosis of thrombosis and occlusion of, 802; dilatation of, 830; diseases of, 777; etiology of purulent inflammation of, 807; etiology of thrombosis of, 787; foreign bodies in, 832; general clinical history of purulent inflammation of, 815; passage of gall-stones into the, 731; pathological anatomy of purulent inflammation of, 813; pathological anatomy of thrombosis and occlusion of, 793; pathology of thrombosis and occlusion of, 798; purulent inflammation of, 805; ramifications of, 6; rupture of, 831; symptoms of purulent inflammation of, 817; symptoms of thrombosis and occlusion of, 799; treatment of purulent inflammation of, 826; treatment of thrombosis

and occlusion of, 804; thrombosis and occlusion of, 785.
Vein, hepatic, ramifications of, 6.
Veins, cancer of hepatic, 834; changes in, in cirrhosis of the liver, 185; dilatation of subcutaneous, in suppurative pylephlebitis, 820; hemorrhoidal tumefaction of, in hyperæmia of the liver, 72; hepatic, diseases of, 833.
Vena cava, inferior lateral pressure in, in etiology of hyperæmia of the liver, 58; perforation of hepatic abscess, 138.
Vena interlobularis, 6.
Vena intralobularis, or centralis, 6.
Venesection, in hepatic colic, 769; in hepatitis, 152; in hyperæmia of the liver, 78.
Ventilation, importance of, in putrid bronchitis, 915.
Vermiform appendix, suppuration of, in etiology of pylephlebitis, 809.
Vesicants, in suppurative hepatitis, 155.
Vesication, repeated, in hepatic congestion, 82.
Vienna paste, in dilatation of the gall-bladder, 645.
Vision, abnormities of, in jaundice, 23.
Vomiting, as a symptom in acute atrophy of the liver, 266, 277; expulsion of gall-stones by, 739.

WALDENBURG'S pneumatic apparatus in interstitial pneumonia, 910.
Water, injection of cold, in catarrh of the bile-ducts, 530.
Waters, alkaline mineral, in the treatment of gall-stones, 774; bitter, in cholelithiasis, 769; bitter, in hepatic congestion, 79; mineral, in amyloid degeneration of the liver, 438; mineral, in catarrh of the bile-ducts, 530; mineral, in catarrhal jaundice, 533; mineral, in chronic jaundice, 631; mineral, in cirrhosis of the liver, 206; mineral, in exudative inflammation of the biliary passages, 556; mineral, in hepatic congestion, 79; mineral, in parasites of the biliary passages, 675; mineral, in suppurative hepatitis, 156; mineral, in the treatment of fatty liver, 471; mineral, in the treatment of gall-stones, 704; sulphur, in hyperæmia of the liver, 80; mineral, sulphurous, in chronic hepatic fistula, 164.
Waxy liver, 407.
Whooping-cough, in the etiology of interstitial pneumonia, 856.
Wine, in cirrhosis of the liver, 207.
Worms, round, in etiology of hepatic abscess, 92.

XANTHOPSIA, 23, 519; in chronic jaundice, 609.

YELLOW FEVER, hemorrhages from the stomach and intestines in, in etiology of jaundice, 18; jaundice in, 28.

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